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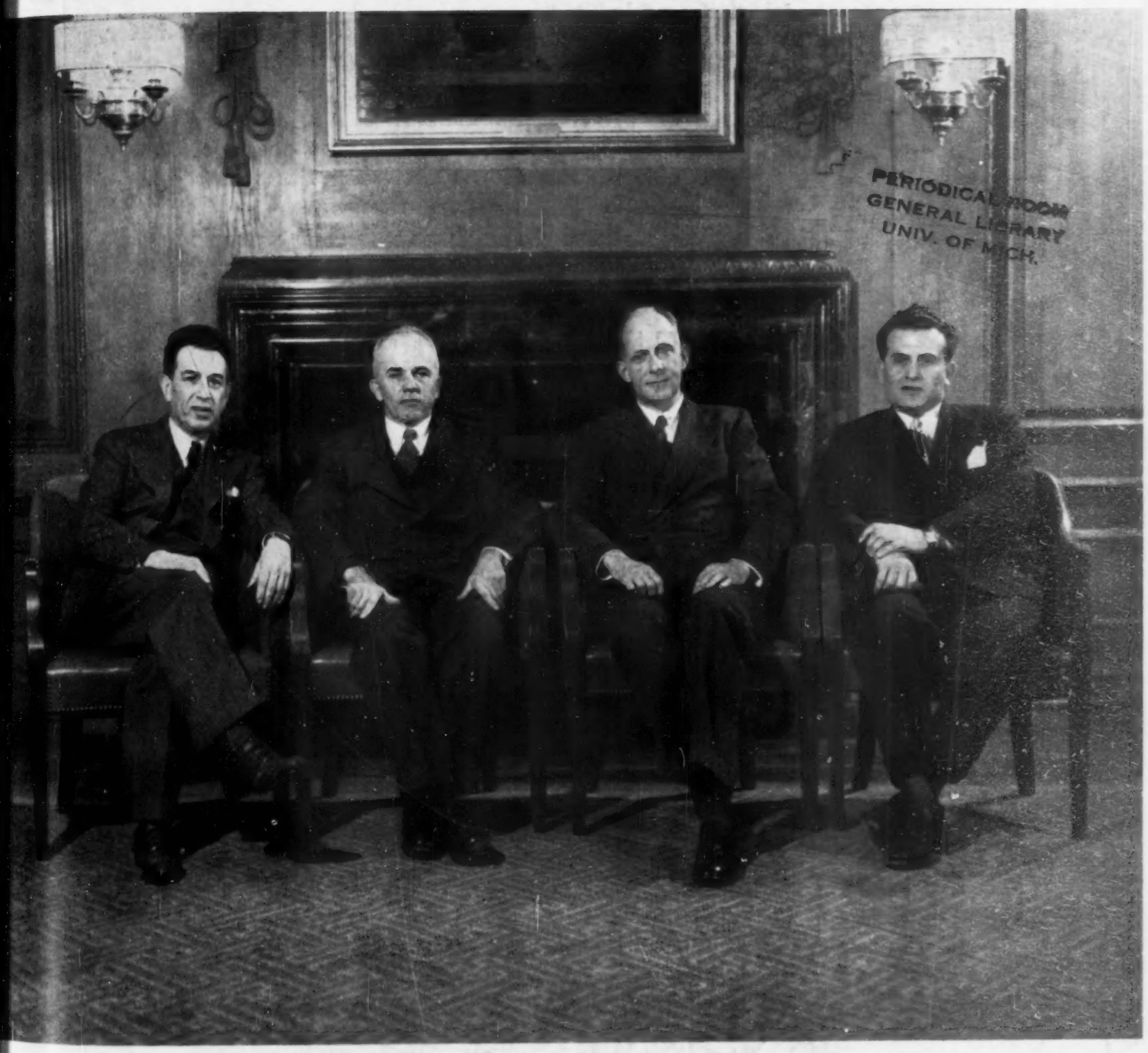

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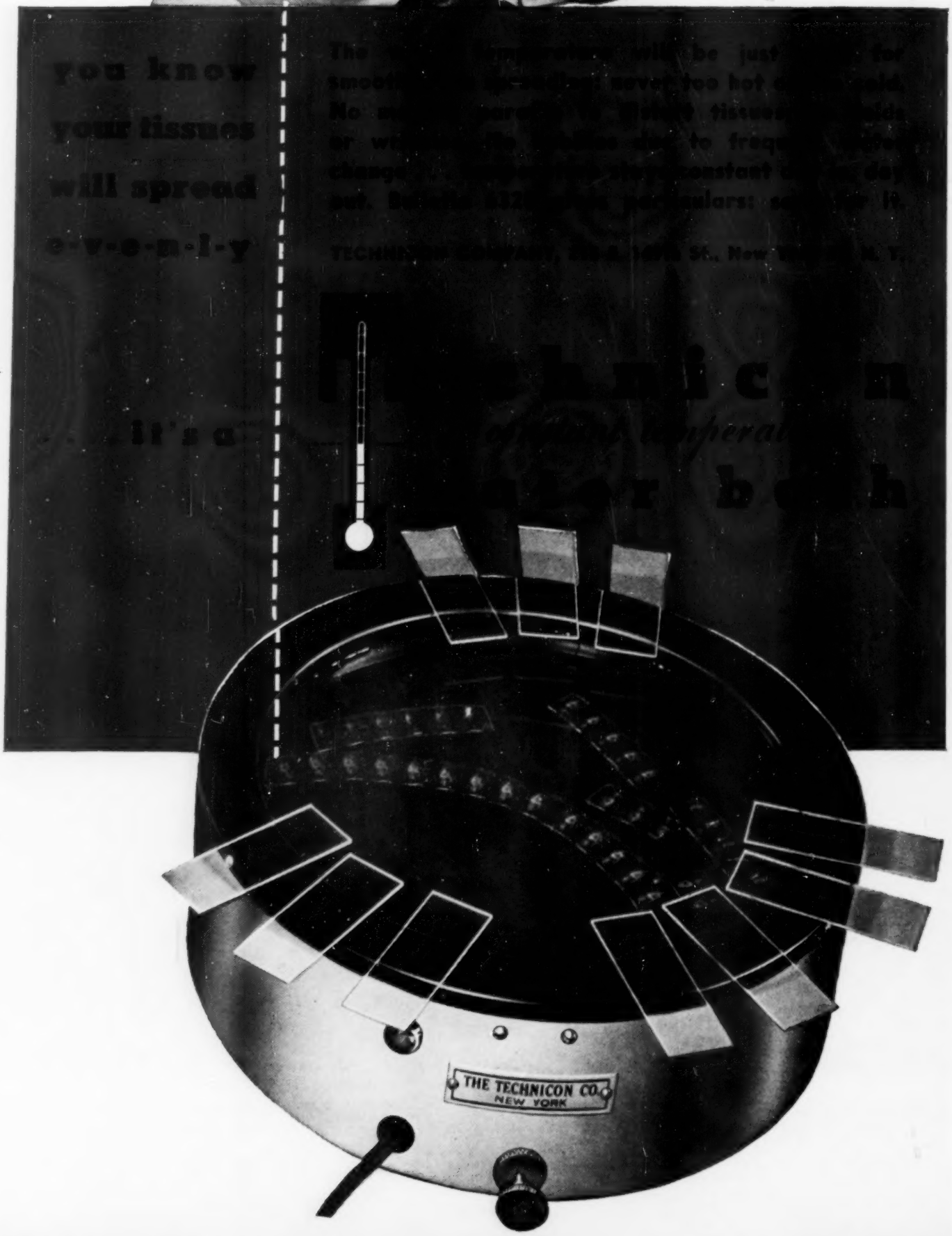

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The Current Transition in the Conception of Science

D. Ewen Cameron

Professor of Psychiatry,
McGill University, Montreal, Canada

THIS PAPER IS CONCERNED with the radical changing of things, with the tearing down and rebuilding of large parts of the understrutting of the world of science in which we work.

By definition, scientists are coldly objective, sternly devoted to the pursuit of their studies, wherever that pursuit may run. Led by Darwin, they set about breaking up other men's pictures of the world. They splintered the proud panorama of Man, the special creation, with all the lesser species spreading out from his feet as lower and lower forms of life. They have joined hands with the great psychopathologists of this century to set in premonitory trembling that image which men have held of themselves as beings guided by intelligence and sustained by a moral order not of their own devising. They have left that Garden, from which all things had seemed to have their origin, nothing more than a warmly smiling fantasy on the face of the enormous reaches of time and space which have been opened up behind us.

Now science itself must face its own bitter catalysis. For in very fact the world of thought is one world; and science, which has wrought such deep changes, must change with them. In this, our discipline, together with the social sciences to which we are so closely related, is a prime mover.

The arbiters of science in the 19th Century were physics and chemistry, mathematics and astronomy. Their language was the language of the universe itself. Their criteria of proof were the absolute in validity; they were the pure in science. In this arid climate the biological disciplines, and more lately the social sciences, have had a hard and bitter struggle to acquire status and, indeed, to win the simple right to the use of the word "science." To this very hour, controversy has not ceased as to whether psychology and psychiatry are true sciences, despite the fact that their discoveries have been among the most profound and moving of our age.

The theory of relativity has fertilized our thought to the liveliest growth. Under its stimulus we have outgrown and destroyed the old concepts of time and space; energy and mass and movement have become interchangeable, and we live in a universe expanding with cosmic speed, or as rapidly contracting, dependent upon the current phase of astrophysical speculation.

Yet when we sit in dispassionate reverie upon our times, we may wonder whether some kindred spirit, far in the future, in like reminiscence upon these days, may not accord primacy in power to the discoveries of our social sciences. I do not refer to those discoveries-to-be with which the midcentury seems clearly to be pregnant, but to those already brought to birth and now in full and busy life.

The insights which psychology and psychiatry have given us have destroyed the absolute monarchy of reason; they are dissolving the ancient concepts of intellect and emotion; the will has almost disappeared.

Before the social sciences grew in power, the world of custom in which we live was a scattering of settlements in a forest of beliefs and folkways which had their roots in the medieval past. To the inhabitants of each little clearing, those outside were the strangers, whose ways of sharing goods, of bringing up children, of living with women, of administering justice, were ways of the foreigner and the savage. Governed by precedent, supported by supernatural beliefs, their aggressions curbed by taboos which they did not understand, they slowly won their battle with the material universe.

Worldwide communication and transportation finally set the field for comparative anthropology. The assertion of each rigid little moralistic system that deviation from its code must bring disaster could be shown to be false, and now the whole moralistic evaluation of human behavior is under question.

But the purpose of this discourse is not to compare the contributions of the physical and social disciplines working within a similar framework of science, but rather to consider how the framework itself is shifting and changing and evolving.

It is shifting—but why? Why should our system of science be changing? The last 100 years have seen incomparable gains in knowledge; those scientific concepts which have been worked out by the four brilliant leaders—physics and chemistry, astronomy and mathematics—have been applied to one field after another with success which has astounded the friends of science and shocked and dismayed its adversaries. The vitalists who declared that organic substances could not be produced without the intervention of vital force

Address delivered before the Ontario Neuropsychiatric Association, Guelph, Ontario, September 19, 1947.

were driven from the scene when Wöhler applied potassium cyanate to ammonium sulfate and formed urea, the first of the great series of organic components which chemistry can now produce at will.

The principle of the reduction of the phenomenon to its elements brought us molecular physics. Then, like a view dissolving and changing as we sweep forward, came the atomic world, and now, the electron and the proton.

Finally, the right of these successful leaders to determine the form and manner of science appeared to be completely vindicated by the results obtained by certain of the new biological disciplines—most particularly, bacteriology. For here the principles of the isolation of the problem from its setting, the controlled manipulation of variables, the use of the deterministic dictum that similar causes are followed by similar effects, led to remarkable successes to which endless numbers of us owe our lives.

And yet its very successes have led to the changing of our conception of science.

At this point in time when the leadership of the basic sciences seemed to have reached the pinnacle of triumphant power, those same forces, the working of which had enabled science to appear, gathered up their strength for a fresh drive forward. What these powers are, we can grasp only in crude and faulty fashion. As we look back over great reaches of time, they appear to be related to, and perhaps derived from, our growing control over our world.

Very early in our history, when we had the lever, the spear, fire, but perhaps not yet the bow and wheel, when we had a few medicinal herbs, but no domesticated animals or agricultural arts, one can see that men attributed human characteristics to all of nature. The river and the hill, the deer and the trees, the wind and the sun, all had traits which man found in himself. Nature could be angered, be propitiated, protect, or exact vengeance.

Immense periods of time passed; man's control over nature grew wider, surer, and step by step his primitive animism gave place to the little gods of life and death—those who presided over the seasons, the gods and goddesses of fertility, of love, of fortune—in a word, those who controlled the happenings which man himself could not yet master.

With still further progress, these little projections of himself gave place to the great one-god systems, which in the last several centuries have been less and less concerned with the direct control of nature. Man was managing this pretty well himself, though whenever there occurred a particularly shattering earthquake, terrifying storm, or destructive drought, there was a return to the belief in the value of propitiation.

The last field which has been left to these systems is our own: that of human behavior—hence, the sharpness of the current struggle between these systems and the social sciences for authority and control over guilt and anxiety, over prohibition and convention, the struggle for direction of the growth of the personality and the ordering of the cultural pattern.

For a vast and rapidly growing number of people our universe now stretches out in endless vistas, neither friendly nor unfriendly to humankind. It awaits our use as we gain knowledge; it can be made to serve our needs without measure and enrich our living in an undetermined degree. If, failing to master our own nature, we turn these waiting powers against ourselves, we shall be destroyed.

These changes in our world image, in the picture which we have of our relations with the environment of men and things, are essential to a successful attack on the problems of human behavior. While men who held anthropomorphic concepts of their world have made great contributions to physics and astronomy, no man can with full effectiveness prosecute scientific studies of human behavior and at the same time maintain beliefs that behavior is subject to unpredictable transcendental control.

I wish now to discuss more specifically the changes which are appearing in our conception of science. They are related in varying degree to this growing confidence with which we deal with our world. The first change is the appearance of new ideas of causality—new concepts of the way in which event may be related to event.

Under the pressure of these vast slow shifts in the relationship between man and his world, changes have been taking place in the very cement which held the old world of science together. The doctrine of determinism had been a tight, hard binding; event was clamped to preceding and succeeding event with rigid unalterability. You had to have it that way. The battle for the lawfulness of the universe had been intense, bitter. Mystic and transcendental interpretations of events have an immensely ancient history. In the old ways of men's thinking, supernatural powers could break in at any point in a sequence of happenings. But if this was to be, there could exist no general scientific laws, there could be no possibility of prediction, and man was back on his knees again, a suppliant and no aspiring master of his world. For the early scientist, event was deterministically handcuffed to event, so that none could escape and nothing unpredictable could break into those long chains.

The scientific worker has now less and less reason to fear that, into his work, into his own thinking, there will once more erupt the ancient magical, the old transcendental, ways. They are all but gone, and what remains is dying.

Once the lockstep had been broken, new patterns of causality began to appear. The biologists freed from this domination were able to see and report that even the simplest of living organisms did not react identically to repeated exposure to what appeared to be identical conditions. They realized that the very fact of response altered subsequent responsiveness, and that living organisms at least must be thought of as continually evolving systems, the future reactivity of which could be predicted only in general outline.

The term organicism was coined to describe this new kind of relationship between the events. Allied to this is the concept of emergent evolution.

The postulates of Gestalt have taken us still further away from the older ideas of straight-line causality relationships and represent, moreover, a revolt against the fragmentation to which the physical sciences subjected their phenomena.

More recently, still other patterns of relationship between events have been discovered. Among them is the concept of the autonomous reaction, a reaction which, once initiated, tends to become self-perpetuating. It has also been described as a circular system, or, less clearly, as a feed-back mechanism, and, as I think quite erroneously and confusingly, as a teleological system. These concepts have been applied with profit to the problem of the perpetuation of chronic anxiety states, to the fluctuation of the population of algae in ponds, and to nonbiological phenomena such as the functioning of thermostats and other servomechanisms.

Before we had discovered these new ways in which event might relate itself to succeeding event, certain problems in behavior were quite insoluble. Before we had come upon the existence of the autonomous, self-perpetuating types of relationship, it was exceedingly difficult to understand the imperviousness of certain of the chronic anxiety states to the usual forms of therapy.

It seems reasonable to anticipate that further exploration of this exceedingly new and provocative field of the various ways in which events may be connected to each other will result in extension of our knowledge concerning such puzzles as the operation of the mechanisms which secure psychobiological homeostasis, often in the face of most considerable stress.

A second consequence of our vast, slow gain in confidence in dealing with our world is our diminishing need for absolutes. This is bringing in its train some highly important changes in our conception of science.

Scientists have long been aware that their facts are in a state of continual revision, and, indeed, in the earlier days when the scientific method was being attacked with more optimism by its opponents, one of the accusations against which scientists had to fortify themselves was that they did not know their own minds until they had read the latest technical journal and found whether yesterday's fact still stood unchallenged. This was usually countered by the declaration that science was concerned with ultimate truth and that its facts represented progressively more reliable approximations to that final truth.

But as we grow bolder, more and more of us are beginning to raise the question of whether the idea of a final truth is not simply a lingering remnant of our urge to anthropomorphize our universe—to provide our anxious-minded selves with some final fixed point. Certainly, nothing in our experience justifies our thinking that there is any such thing as an ultimate.

Hence, a number of workers are now beginning to discard a whole network of 19th-century scientific concepts—the ultimate truth, the scientific fact, the so-called laws of nature. In their stead, they are beginning to think of the fact as the working hypothesis of the day, which has not a validity but a utility. That utility consists in its effectiveness in expanding our control over events, and it lasts only until a better working hypothesis can be found.

The laws of nature are now considered simply to represent our ways of conceptualizing data, and the absolute is seen as our need for security.

A number of men are now feeling confident enough to work in an open rather than in a closed system. By an open system, I mean one in which there are no final facts, no unchanging truths, where everything is relative and conditional and, above all, fluid and plastic.

This group of changes in the conception of science is likely to bring with it consequences of considerable vitality, for if we can free ourselves of our beliefs in the ultimate and the final in the scientific field, we can anticipate that through the usual processes of the migration of concepts there will be a crumbling of similar beliefs in the inevitable and absolute in other fields.

It is everywhere recognized that we are approaching a crisis of the first magnitude in our affairs. We have been unable to produce the social adaptations and inventions necessary to meet the changes forced upon us by our industrial and material progress. What is not so clearly recognized is that we have not found adequate means or, indeed, sufficiently potent social sanctions to enable us to break up and remove ancient, outmoded beliefs and social institutions. Hence, the penetration of these new concepts, concerning the unreality of the absolute, from the scientific field into everyday thinking would be a most outstanding gain.

Perhaps most people, when asked to say what they consider to be the chief value of science, would answer that it was to discover the causes of things. But it

does not seem likely that we will continue to believe this. Indeed, the whole idea of causes is now a much less clear-cut affair than it was two generations ago. The early bacteriologists, the pioneer endocrinologists, and those who worked in the new field of the vitamins were very sure that their great contributions were the working out of causes. Occam's razor—you may not multiply explanations unnecessarily—and the then-existing concepts of causal relationships partnered to produce the idea of the single cause.

Hence, in our field there was a long delay in recognizing that behavior could be conceptualized as an interaction between the total individual and his total environment. For decades, workers continued to seek to define specific reactions and specific causes. Modification came from a series of compromises, the more important being the Meyerian ideas of multicausal etiology and of action tendencies, rather than specific reactions—or diseases.

Now we are approaching a period when the whole concept of the cause may be abandoned in favor of a hypothesis of chains of event sequences continually interacting with, and modifying, each other. Causes, then, are seen to be no more than our recognition of places in these sequences at which we can most successfully interfere, either now or when we have gained more skill.

It is certainly true that in actual practice, even when we continue to think of causes and designate one of these as primary, we rarely attempt to control the situation by trying to modify the primary cause. The explanation of this is simple: such modification is impossible, since the primary cause is no longer operative.

Let us turn now to a procedure which scientists have used very widely in getting their projects ready for investigation. This procedure is that of abstraction.

The behavior of the 19th-century scientists at work on a problem is reminiscent of a dog with a bone. He dragged it off from wherever he found it to some secluded place of his own choosing. In the laboratory, the world, with all its contaminations, its uncontrollable variables, its uncertainties which simply would not submit themselves and be quantified, was shut out. It is amazing that, under such circumstances, what man worked out from his highly abstracted version of the original problem did have any validity at all when transferred back to the setting from which the problem originally had been lifted. Of course, often enough it did not, and the path between the laboratory and the industrial plant is just as liberally paved with good scientific intentions as was said to be that Hell of our guilt-ridden ancestors. A substantial measure of this difficulty of retranslating from the scientific abstraction to the actualities of scientific production is the existence of the pilot plant as the place of adaptation between the test tube and the production line.

This device of abstraction is difficult enough to apply to problems of chemistry, electricity, or magnetism. It becomes more difficult when we apply it to the living organism, and almost impossible when we try to use it in studies upon the behavior of groups of living things. It is customary to explain this difficulty by saying that it stems from the fact that such problems involve the control of far more variables. This is only a small part of the answer. Anyone even vaguely familiar with the complexity of matter, as now understood, can have no doubts of the great range of variables to be controlled in chemical and physical problems. The difficulty seems rather to lie in the fact that the living organism is essentially adaptive. Hence, the problems which we wish to study are compounded of the organism and its setting. If one lifts the organism out of its setting to transport it to the laboratory, the problem is ruptured.

At this point we return to what has already been said, namely, that the Gestalt approach, with its emphasis upon wholes, is the answer of the social disciplines to the elementarism of the basic disciplines.

An answer which is still lacking is how we are to rewrite the criteria of proof. The experimental method as elaborated by the physicists and chemists, and later by the bacteriologists and the animal physiologists, was a tool magnificently effective in meeting the needs of validation. We are learning how to apply it, how to modify it, for our purposes in the social sciences. We have long since redirected our attention from the immense regularities and averages to the study of individual differences. We have the beginnings of a statistics of small samples. But no one can feel satisfied with the validation of many of the concepts which have been advanced in our field during the last several years. Their only present justification is empiric. Progress has been made, however, and it can no longer be asserted that abstraction and isolation of the problem is an essential part of the scientific method.

Thus far we have discussed changes in particular aspects of the conception of science—changes in our ideas concerning causality, concerning the usefulness of the idea of cause, concerning absolutes, the replacement of a closed system by one that is open, and we have talked about profound modifications in the theory of the experiment. All these marshal great power and will bring about the most extensive reordering of our conception of science and, from this, of our image of the universe. But they are parts and systems within the whole, and change now impends not

only for these components but for the over-all conception of science with which we passed out of the 19th Century. This was brought into existence during a period when it was urgently necessary that this new way of dealing with things should be separated as sharply as possible from the previous subjectivism, from the all but overpowering effects of traditional beliefs upon men's thinking.

Every effort was made to assert that science was a system which had a reality apart from the men who built and operated it. Hence, we have this curious inversion, the laws of nature which men sought to discover. It was a little like hunting a thimble which you yourself had hidden, because very certainly the laws of nature have no existence in themselves; they are simply the ways in which we find it convenient to conceptualize phenomena.

One of the earliest pieces of evidence that science was not a system, but a form of behavior, was a small discovery made, as it were, in a corner of that ordered world of science which had been fathered by the physical disciplines. This evidence was the "probable error," or, as Bessel, that sensitively perceptive astronomer of Koenigsberg, preferred to call it, the personal equation. Small though this discovery may seem, it was of great significance not only as a forerunner but in its own right. One may feel that to record the fact that a number of observers, watching the transit of a star under identical conditions, will report divergent readings, is a matter of importance only to those interested in the refinement of measurement. But of far greater meaning is the fact that it heralds the recognition of the human factor in science. It means that science can no longer be considered a machine which may be set in motion without any regard for the man who operates it.

Starting from the probable error, and passing through the minds and work of a great series of animal experimentalists, biologists, and social scientists, we are now emerging with an entirely new conception of science, namely, that it is a form of human behavior comparable to sexual behavior, economic, family, or industrial group behavior.

This at once opens up considerations which carry with them very far-reaching consequences. First, we must question to what extent our own innate organization determines the nature of our scientific behavior. Most assuredly it does. But how, and to what degree? Almost all of this new ground is highly speculative, and I shall discuss it as such. We are greatly plagued, both in lay thinking and in our scientific work, by the tendency to use dichotomies—good and bad, introvert and extrovert, conscious and unconscious, higher and lower functions. How far is this dependent upon the fact that we exhibit in ourselves the phenomena of sidedness? You will recall a number of schizophrenic patients who convert sidedness into just such terms as I have used. They refer to the right side as good, and to the left as the side on which they have fallen down—the bad side.

To what characteristics of the organization of our natures is due the fact that we have so much more difficulty in dealing with the abstract than the concrete? On this we have no data, and speculation has barely begun. Those very characteristics of our nature which have been responsible for our astounding progress as a species have carried with them hidden detriments. It is true that our adaptability is immensely greater than that of any other living creature. We are the animals which have taken a chance; we left the shelter of the trees and then the protection of the caves; we played with fire; we crossed the perilous seas; we have dared to leave the earth. Other animals have chosen to adapt themselves to circumstances and have produced protective coloring, speed for escape, armor for defense, and prolific fertility for survival. We have never made that choice. We have come to our problems without ready-made solutions, relying on our ability to work out answers on the spot.

While this has given us great gains, it has been at the cost of great anxiety and insecurity. It has been necessary to build up worldwide reassurance illusions, which in turn have slowed the progress of science. We can see this at a glance in our fairy tales, in the folk stories of powerful figures, in our father-image myths, beliefs, and creeds. Many of the effects of this species insecurity are less immediately obvious. To illustrate this, we may turn to the field of remembering, where the progress of our knowledge has been delayed by such lay beliefs as that the past is with us, that we can relive it, that by far the greater part (indeed, some of our psychopathologists believe, all) of what we experience is stored away as memories. In actuality, by far the greater part of what we experience is lost forever, and that within a few minutes. But we have an overpowering need to preserve our sense of identity, of fixity, in this rapidly changing world—hence, this illusion.

Of at least equal importance is another consequence of our new conception of science as a form of human behavior. We are beginning to appreciate the extent to which our cultural endowments influence both the range and acuity of our conceptional abilities. Everywhere anthropologists are showing that the people of a given culture may be able to develop certain concepts but not others, and that this has nothing to do with their innate ability but a great deal to do with the way in which their upbringing within the culture affects their capacity to conceptualize things.

The Mayas were able to create architectural and

agricultural arts of a high degree of excellence. They developed a calendar more accurate than ours, and they devised a highly original system of mathematics. But amazingly enough, though they carried on this most successful agricultural society, they were quite incapable of inventing the plough.

We may well question why the Romans, who were such capable administrators, military experts, road and bridge builders, should have been unable to produce a power-industry civilization. We may go further and say that the basic concept was actually in existence, but that it simply could not be expanded and applied; for, in 130 B.C., Hero of Alexandria described in his "Pneumatica" at least two methods of harnessing power to steam.

We have been inclined to obscure this puzzle as to why scientific and industrial development came so late by considering that these earlier periods were somehow representative of the youth of our species—and, as everyone knows, the boy really does become smarter when he grows up. This might be a simple way out if we still believed that we originated in 4004 B.C. But now that we know that the first traces of man go back for at least half a million years, we have to think of the Romans almost as contemporaries. This concept of cultural indoctrination as affecting scientific behavior as well as all other forms of behavior has, of course, immediate significance. We shall want to know to what extent current indoctrinations—political, nationalistic, religious—limit our ability to conceptualize our world and, thereby, hinder the progress of our control of our universe through science.

I have tried to show through what vistas we have the scene of the extremely interesting and provocative things which are happening to our conception of science. It is the inmost germinal place of our future.

I reiterate my belief that psychiatrists, with their unique position between the medical and social sciences, have a special responsibility to act as leaders and guides in entering and opening up this new territory. We have the responsibility not only to create the new tools and the new concepts but we also have a most serious duty to assist in finding means to destroy the old and the obstructionist. It is one of the graver lessons of our times that the new, the more liberal, the more effective, does not immediately succeed without our active assistance in driving out the old, the harmful, and the entrenched.

Obituary

Burton Edward Livingston
1875-1948

Burton Edward Livingston began his career as a botanist at a very early age in the fields and woods, along the ponds and streams in the vicinity of his home in Grand Rapids, Michigan. Early experiences with trees, flowers, and the general flora of his native region undoubtedly exerted a strong determinative influence upon his life. His parents and older brothers and sisters were unusually interested in plants, their habitats and behaviors. This home environment must have been a powerful stimulus to his development.

In addition to contacts with the flora of central Michigan, he had an opportunity to become familiar with all kinds of tools and machinery, for his father was a contractor in the street-paving and sewer-construction business in Grand Rapids.

A third factor which helped to shape his background development was the home library, which was quite out of the ordinary at that time. Burton acquired the habit of reading rather widely and became omnivorous in his literary tastes. He also had the privilege of playing with simple microscopes and of becoming familiar with their use before he ever attended school. All of these factors had a definite bearing upon the course of his life and helped to create that interest in the plant sciences which made him later on a great leader in the fields of plant physiology and forest ecology.

Grand Rapids was the scene of his grade and high school training. In the high school he had the good fortune to learn the fundamentals of many sciences, as well as a number of languages which would be useful to him as a leader of research in his chosen field. He began making an herbarium in high school and afterwards continued to collect plants as a scientific project. Having gone far beyond the requirements for school work, he acquired a wide acquaintance and knowledge of the plant kingdom and, upon entering the University of Michigan, was rewarded by being given 10 hours of advanced credit in botany for his herbarium activity.

When he was old enough to engage in gainful employment, he obtained a job at the Pitcher and Manda United States Nurseries at Short Hills, New Jersey. The year he spent at Short Hills gave him the oppor-

tunity to learn every operation that a great nursery requires. This was an invaluable experience for a young man turned toward scientific problems. He left the nursery in the early summer of 1894 and spent the remainder of that summer botanizing and adding largely to the herbarium, which had by this time become a very considerable collection.

In the autumn of 1894 he entered the University of Michigan, where he had the good fortune to work with such outstanding botanists as V. M. Spalding and F. C. Newcombe. It was the latter who turned Livingston decisively into the field of plant physiology. After a year of study, he became Newcombe's laboratory assistant. In a sense, that was the beginning of his career as a plant physiologist interested in plant habitats and distribution and in the impact of soils and climates upon plant behavior. He took naturally to the problems of plant physiology as modified by environmental complexes of temperature, light, humidity, and wind flow, which were recognized as dynamic systems. Soil conditions and plant growth also challenged his interest. Altogether, these were fields of unlimited ramifications and possibilities.

During the Ann Arbor period there was a visit to New York, where he met N. L. Britton and John K. Small, both of whom proved to be very stimulating. In 1898, having completed the undergraduate work at Michigan, he was awarded the B.S. degree and began teaching at the Freeport, Illinois, high school. In the midst of his first year of teaching, he applied for fellowships at a number of universities. Among several that were offered to him, he chose to accept a fellowship and assistantship in the Department of Botany of the young, but already famous, University of Chicago. He entered Chicago in the summer of 1899 and became the first of a distinguished group of men who assisted Charles Reid Barnes in the plant physiology laboratory there.

Although Livingston completed his work for the Ph.D. degree in 1901, he remained as laboratory assistant and associate in botany until 1905. His book, *The rôle of diffusion and osmotic pressure in plants*, published by the University of Chicago Press in 1903, is still an important summary of the field up to that time. It was during this period at Chicago that the writer was first privileged to know him as a tall, friendly, earnest young man who was adept in all of the techniques used in the study of plant physiology.

Beginning in 1905, Dr. Livingston held various positions which must be thought of as preparatory for his real life work. For a part of the year he was in charge of fertility investigations in the Bureau of Soils, U. S. Department of Agriculture, Washington, D. C. In 1906, the Carnegie Institution of Washington, which was just getting well started, offered him a position as staff member of the Department of Botanical Research, which he accepted. He went to Tucson, Arizona, and found conditions around the Desert Laboratory a great challenge to his interests. Here he first developed and used the porous porcelain atmometers in studying the evaporativity of the plant environment and the drying influence of sunlight. Then followed a year at eastern institutions and at the Missouri Botanic Garden, where he studied particularly the transpiration of greenhouse-grown cacti. In 1908 he traveled in Europe, spending time mainly with von Goebel at Munich, but visiting Pfeffer's institute at Leipzig for several weeks, Klebs at Heidelberg, and Hall at the Rothamsted Agricultural Experiment Station in England. He returned from Europe late in 1908 and attended the Baltimore meeting of the AAAS. At this time he first saw D. S. Johnson's Botanic Garden at Homewood, which was just becoming the home of Johns Hopkins University. He returned to the Desert Laboratory, but in 1909 he was invited to accept the chair of plant physiology at Johns Hopkins and promptly accepted the offer.

In estimating the personal influences most important to him during these years leading up to the Hopkins appointment, Dr. Livingston always acknowledged his special indebtedness to Newcombe, Barnes, Cowles, and Jacques Loeb.

In 1913 Dr. Livingston was made director of the Laboratory of Plant Physiology at Johns Hopkins, a position which he held with great distinction until 1940. In 1932, forest ecology was added to his field. As soon as the Johns Hopkins Laboratory of Plant Physiology was opened, it became a sort of mecca for plant physiologists, not only from the United States but also from far-distant lands. About 140 graduate students were enrolled in advanced work in the laboratory during the period 1909–40; of these, there were 28 Ph.D. candidates who successfully met the requirements and obtained degrees.

Livingston's contributions to the advancement of science were many and varied. He and his students published nearly 300 papers during the tenure at Johns Hopkins. These papers were especially valuable because they presented full discussions and masterly integrations of the old and new knowledge which illuminated the whole field covered. Such problems as temperature, light intensity, 3-salt nutrient solutions, the continuous renewal of culture solutions, foliar transpiring power, the daily march of transpiration, the seasonal march of soil moisture conditions, the water-supplying power of soils in relation to the wilting and withering of plants, the carbon dioxide-supplying power of the air, and the oxygen-supplying power of soils and its relation to seed germination are representative examples of topics pursued in the

wide-ranging quest for new understanding which went on continuously in the Laboratory.

At the same time, Dr. Livingston contributed to the advancement of plant physiology and ecology by the invention or improvement of many excellent instruments for measuring the effects or intensities of dynamic environmental factors. The porous porcelain atmometers, cylinders, spheres, and plates, in both black and white, with standardized techniques, made possible more accurate measurements of the evaporativity of environments. Batteries of black and white spheres went all over the world to help ecologists and physiologists to evaluate the effects of atmospheric humidity and sunlight upon the water relations of plants. Auto-irrigators provided means of control for soil moisture conditions in pot culture experiments; soil points of porous porcelain were invented to measure the water-supplying power of soils. These soil points were extremely accurate in their readings when they were used at some definite hygrometric water content.

In addition to these various porous instruments, he made and sold to laboratories many supplies that could not be obtained elsewhere. These included leaf clips used in transpiration experiments, hygrometric paper, permanent color standards, tripartite color standards, and standard evaporating surfaces with which leaves could be compared. A reconditioning service was maintained to clean, rewaterproof, and restandardize apparatus for laboratories not equipped to perform these necessary operations for themselves. These instruments and services were widely used, and thus the influence of the Johns Hopkins Laboratory was extended to many lands.

In addition to the book published in 1903 and his numerous scientific contributions in journals, he published with Forrest Shreve a book on *The distribution of vegetation in the United States as related to climatic conditions* (1921). In 1918 he edited an English translation of Palladin's *Plant physiology,* which appeared in three editions by 1926.

Dr. Livingston was a skillful editor, and he contributed to various journals in an editorial capacity. Notable among these were *The American Scholar, Physiological Researches, Botanical Abstracts,* and *Plant Physiology.* He exerted much influence on the editorial policies of the latter journal, upon whose editorial committee he served for many years. He deserves a great deal of credit for the general excellence of appearance and contents of the early volumes of *Plant Physiology.*

It would be difficult to overstate the value of his services to the American Society of Plant Physiologists in the first few years of its existence. Although he was not a prime mover in its organization, he was very sympathetic toward its ideals, and it was through his interest and advice that the new society was affiliated with the AAAS in October 1924, before the Society was 6 months old and before it had held an annual meeting. Affiliation gave the plant physiologists representation on the Association's Council. Many were the times that Livingston's advice and encouragement steered the new Society away from the reefs. So important were his contributions that when the Charles Reid Barnes honorary life memberships were established at Kansas City in 1925, Dr. Livingston was chosen to be the first recipient of this honor at Philadelphia in 1926.

In 1927, when the Society celebrated the Stephen Hales anniversaries at Nashville by founding the Stephen Hales award, Dr. Livingston made the largest single contribution to the fund for the Hales endowment, and it was made in a manner to encourage generous giving by others.

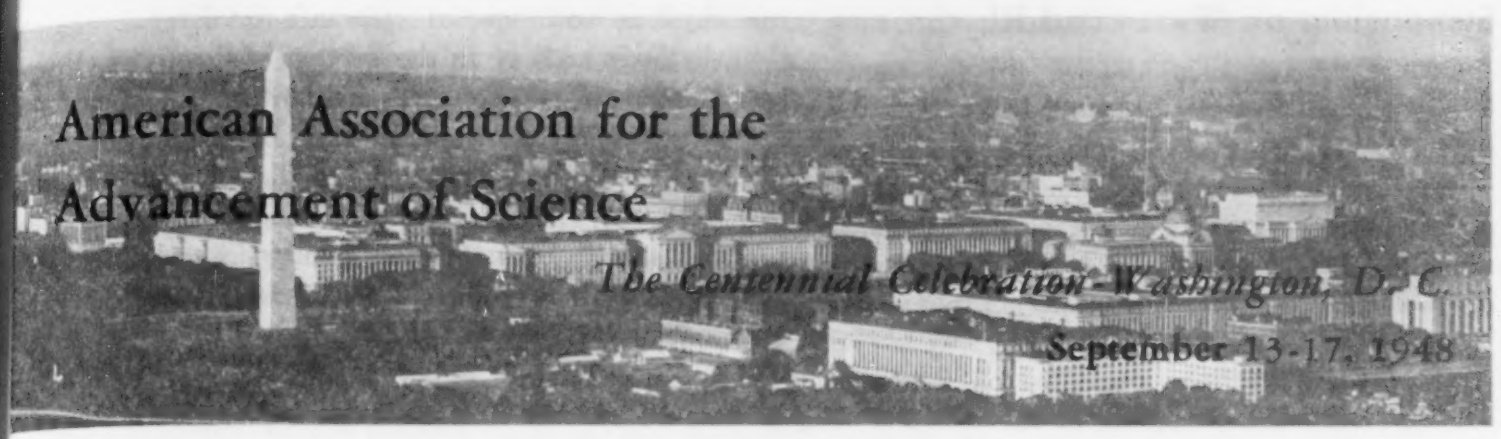
In 1934 he was elected president of the American Society of Plant Physiologists. During that year the constitution was revised, and many changes were made in the procedures, all in the direction of more liberal and democratic management of the Society's affairs. His long-continued interest and his vital contributions to plant physiology through the Johns Hopkins Laboratory finally led to his selection as recipient of the Stephen Hales award in 1946. He was too ill by December 1947 to deliver his address in response to this award at the annual meeting of the Society.

Although he belonged to many organizations, his first love and loyalty was the American Association for the Advancement of Science. He became its permanent secretary in 1920 and served for three successive terms, until 1931. During his secretaryship the Association grew rapidly. It was the writer's privilege to be associated with him in the office of the Association in Washington and also in the Johns Hopkins Laboratory, for a few months in the autumn of 1923. It was always a marvel to me how one man could carry two such man-sized obligations without apparent physical impairment. Dr. Livingston seldom admitted that he was tired, yet he always carried a burden too heavy for one man's shoulders. He served the Association for three years as general secretary (1931–34); and throughout the whole period of his connection with the Association, he was a member of its Executive Committee, helping to shape its policies during a long period of phenomenal growth. Few men have served the Association so long and so well.

Dr. Livingston's death on February 8, 1948, leaves his many students, colleagues, and friends, who were legion, with a deep sense of personal loss.

CHARLES A. SHULL

42 Oakwood Street, Asheville, North Carolina



Afternoon Activities

One of the unusual features of the celebration in September will be the opportunity to see "One World of Science" as it is illustrated in action in the Nation's capital. The Government of the United States has a tremendous investment in scientific research, and although a major part of it is carried out elsewhere, it is only in Washington and its vicinity that examples of nearly every type may be found.

More than 40 institutions which are cooperating in arranging local functions will be hosts to visiting scientists. These include the universities—American University, George Washington University, Georgetown University, Howard University, and the University of Maryland; societies affiliated with the AAAS which have headquarters in or near Washington—Academy of World Economics, American Association of Economic Entomologists, American Chemical Society, American Home Economics Association, American Pharmaceutical Association, American Psychological Association, American Statistical Association, Metric Association, National Association of Science Writers, National Education Association, Society of American Foresters, and Society of Rheology; governmental organizations—Bureau of Agricultural Economics, Bureau of Animal Industry, Bureau of Entomology and Plant Quarantine, Forest Service, U. S. Coast and Geodetic Survey, Weather Bureau, National Bureau of Standards, Bureau of Mines, Fish and Wildlife Service, Food and Drug Administration, National Institute of Health, U. S. Office of Education, U. S. Public Health Service, David Taylor Model Basin, National Naval Medical Center, Naval Ordnance Laboratory, Naval Research Laboratory, National Academy of Sciences, Office of Naval Research, U. S. Naval Observatory, National War College, Library of Congress, and Smithsonian Institution; and other organizations—Carnegie Institution of Washington and National Society of the Daughters of the American Revolution.

For relaxation those attending the celebration will have an opportunity to make unscheduled trips to many art galleries, libraries, museums, and historic monuments located in Washington. A guide to these and a map of the city will be given out at the time of registration. Since no activities have been scheduled for Monday afternoon, September 13, those arriving in Washington early may avail themselves of this opportunity to study the superb cultural displays situated along the capitol mall. The opening session will not commence until 8:30 P. M., Monday evening, in Constitution Hall, allowing sightseers ample time to rest between the closing hours of governmental buildings and the start of the evening event.

Special tours of institutions engaging in scientific research are being planned for the afternoons of Tuesday, Wednesday, and Thursday, September 14 through 16. The National Institute of Health, the Agricultural Research Center at Beltsville, the National Naval Medical Center, the National Bureau of Standards, and many others will welcome visiting scientists and their families and conduct them on inspection trips through laboratories housing demonstrations that feature current research programs. Those wishing to participate in these tours may make their reservations at the time of registration. A schedule of trips to institutions will be published in the announcement of the meeting which will be mailed soon to members of the Association.

There will be much to attract specialists who may desire to see advancements in their own fields of science, but the important purposes of the afternoon activities will be to enlarge the horizons of all who participate in the Centennial Celebration, to bring together educators, research workers, and others interested in advancing human welfare, and to facilitate cooperation among them.

As chairman of the Afternoon Activities Committee it is a great pleasure to invite the members of the Association and the members of its affiliated societies to join in the commemoration of the founding of the AAAS and to extend to them a cordial invitation to visit the great scientific and cultural institutions in and about Washington. (RAYMUND L. ZWEMER, *chairman of the Afternoon Activities Committee.*)

Symposium on Waves and Rhythms

One of 15 symposia planned for the Centennial Celebration is to deal with the subject of waves and rhythms. If nature ever abhorred a vacuum, she seems to love waves and rhythms. Rhythmic events are characteristic of many phenomena, ranging from social, political, and economic cycles, through a variety of biological rhythms, to radiation phenomena in chemistry and physics.

Three papers will be presented on September 14 dealing with selected aspects of this subject. James B. Macelwane, S.J., will consider rhythmic events in the earth's crust from the point of view of a seismologist. Dr. Macelwane is professor of geophysics, dean of the Graduate School, and dean of the Institute of Geophysical Technology at St. Louis University. He is a member of the National Academy of Sciences and author of several books and many papers on seismology and related subjects.

Hudson Hoagland will consider aspects of biological rhythms with special reference to determinants of rhythmic activity in the nervous system. Dr. Hoagland, who is executive director of the Worcester Foundation for Experimental Biology, neurophysiologist at the Worcester State Hospital, and research professor of physiology at Tufts Medical School, is the author of numerous publications dealing with aspects of neurophysiology and the physiology of time.

A third aspect of waves and rhythms will be discussed by Vern O. Knudsen, a student of the physics of sound and of supersonics, who has made outstanding contributions to problems in the field of audition. Dr. Knudsen is professor of physics and dean of the Graduate Division of the University of California at Los Angeles. He has served as president of the Acoustical Society of America and in 1934 was awarded the $1,000 prize of the AAAS. In addition to many scientific papers, he is the author of the books *Architectural acoustics* and *Audiometry*.

NEWS and Notes

Abraham White, associate professor of physiological chemistry at Yale University, has been appointed professor and chairman of the Department of Physiological Chemistry in the new School of Medicine of the University of California at Los Angeles. Dr. White, who has been a member of the Yale faculty since 1933, received the Eli Lilly Prize Award in Biochemistry in 1938. He will take up his new duties on July 1.

William W. Flexner, professor of mathematics at Cornell University since 1934, has resigned, and in June will take over his new duties as senior statistician in charge of transport statistics for the Department of Economic Affairs of UN.

Lewis W. Beck, associate professor of philosophy at the University of Delaware, has been appointed professor of philosophy at Lehigh University, effective September 1.

Robert F. Griggs, professor of biology, University of Pittsburgh, will serve as consultant to the University of California during the summer months. Dr. Griggs will advise the University on the use of fire as a tool in the management of Brush Ranges.

Peter L. Bellaschi, formerly with the Westinghouse Electric Corporation, has recently become engaged in consulting work. Mr. Bellaschi, who has lectured before engineering groups in this country, Europe, and South America, has been active in the fields of transformer development, lightning research, transmission, standardization, etc. He is presently located at Sharon, Pennsylvania (P. O. Box 403).

C. J. Mackenzie, president of the National Research Council of Canada, has been appointed president of the Atomic Energy Control Board, succeeding Gen. A. G. L. McNaughton.

A. L. Pickens, professor of biology, Brenau College, reports that contacts have been re-established with **Otto Porsch,** of Vienna, author of numerous works on pollination of flowers by animals and especially by birds. Associated with the Hochschule für Bodenkultur, he had, by the late 1930s, published a number of papers on the less familiar subject of mammalian pollinators. Although Dr. Porsch has reached the age of retirement, he hopes to continue research in his favorite field.

Ford M. Milam, former research assistant in soils and crops at North Carolina State College, whose appointment as coordinator of agricultural education and research under the American Military Government in South Korea was announced in *Science,* December 19, 1947, has been elected vice-president of the Korean Agricultural Scientific Society "in recognition of his services to scientific research in agriculture in Korea." The Society, of which Cho Paik Hyun, dean of the Suwon College of Agriculture and Forestry, is president, is a group of outstanding Korean and American scientists similar to the American Society of Agronomy.

Ralph M. Hixon, head of the Department of Chemistry and director of the Corn Research Institute, Iowa State College, has been named new dean of the Graduate College. Dr. Hixon succeeds **R. E. Buchanan,** whose retirement on July 1 has been previously announced.

Bradford B. Hudson, after service as psychologist with the Office of Strategic Services and the Central In-

telligence Agency, has been appointed assistant professor of psychology at the Rice Institute, Houston, Texas, effective in August.

Harold E. Way, who has been head of the Physics Department at Knox College since 1937, has accepted appointment as professor of physics and head of the department at Union College. He succeeds **Vladimir Rojansky**, who will devote full time to teaching and special research projects.

Harlow Shapley, director of the Harvard College Observatory, has been elected an Honorary Foreign Member of the Royal Irish Academy of Dublin. The Academy was founded in 1789 and has a total membership of approximately 200.

Colleges and Universities

A collection of allergenic pollen and specimens of all plants producing hay fever throughout the United States is being undertaken under the auspices of the American Academy of Allergy by the University of Illinois College of Pharmacy. Ralph F. Voigt, associate professor of pharmacognosy and pharmacology, will be curator of the collection, the samples and specimens being received and kept at the College's proposed Drug Plant Experimentation Station, to be located at Lisle, Illinois. An Academy subcommittee consisting of O. C. Durham, chief botanist of Abbott Laboratories and also a member of the faculty of the University of Illinois College of Pharmacy, A. O. Dahl, of the University of Minnesota, and Dr. Voigt will supervise the collection. As slides of the various pollens are made available, physicians and research workers in this field will be able to obtain them for use in their studies.

Richmond Professional Institute, a division of the College of William and Mary, will add to its curriculum next September a four-year course designed to prepare students for employment in the chemical industry. This course, which was planned by Mary E. Kapp, chairman of the Chemistry Department, and C. W. West, assistant professor of chemistry, in cooperation with I. J. Krepick, director of business administration, will combine basic information in chemistry and physics with essentials of business administration. In addition to year courses in general chemistry, qualitative and quantitative analysis, organic and industrial chemistry, physics, and mathematics, appropriate business subjects, psychology, and English will be taught. Having obtained the B.S. degree in chemical technology at the conclusion of the course, students should be equipped for entrance at an apprentice level to the marketing, market research, sales, and advertising divisions of industries where chemistry plays a major role.

A series of lecture-demonstrations for teachers of physiology or pharmacology, extending from July 5 to 10, will be given in the Department of Physiology, New York State Veterinary College, Cornell University. The course was recently announced by private communication to physiologists and pharmacologists. Space for several more persons at the demonstrations is still available. There will be no fee for visitors attending the meetings. Further information may be obtained by writing to H. H. Dukes, Department of Physiology, New York State Veterinary College, Cornell University, Ithaca, New York.

A portrait of Lewis H. Weed was presented to the Johns Hopkins University on May 14 by a group of his friends numbering more than 330. The picture, painted by John C. Johansen of New York City, will be hung in the Welch Medical Library. Dr. Weed, who was appointed professor of anatomy at Johns Hopkins in 1919, dean of the Medical Faculty in 1923, and director of the School of Medicine in 1929, recently retired from his university posts to devote full time to the chairmanship of the Division of Medical Sciences, National Research Council.

The Oklahoma Baptist University library has announced the addition of 513 new items to its geology collection. The gift, made by Frederick J. Smith, of the Sinclair-Prairie Oil Company, includes books, reprints, monographs, and scientific journals. Earlier this year, the collection was given several thousand volumes by oil and mining companies and many of the state geological surveys.

Meetings and Elections

At the convention of the Biological Photographic Association, to be held September 8–10 in Houston Hall, University of Pennsylvania, Philadelphia, there will be an interesting exhibition of prints, color transparencies, and motion pictures in the field of biological photography. As an innovation, organized symposia and demonstrations are planned. Edmund J. Farris is president of the convention, and Harry E. Morton is chairman. Further information about either the Association or the forthcoming meeting can be obtained from: Secretary, Biological Photographic Association, University Office, Magee Hospital, Pittsburgh 13, Pennsylvania.

La Société de Chimie Biologique is in process of organizing its 8th Congress, which will be held in Paris, October 6–8, and which will be the first international gathering of general biochemists taking place in France in the last 10 years. The Organizing Committee hopes that the Congress will be as successful as that held in Liège in 1946. In addition to sessions devoted to Proteins and Enzymes (MM. Theorell and Fromageot), Organic-biological Chemistry (MM. Stoll and Janot), and Vitamins and Hormones (MM. Dodds and Horeau), there will be sessions on other subjects, demonstrations, and various social functions. Further details concerning the program and reservations may be obtained from Jean Courtois, Secretary of the Congress, 4, avenue de l'Observatoire, Paris 6, France.

Science Service has recently announced the election of two new trustees, Karl Lark-Horovitz, chairman of the Department of Physics, Purdue University, and general secretary of the AAAS, and Charles E. Scripps, of Cleveland, Ohio. With the exception of the AAAS, which still has one trustee vacancy, the National Academy of Sciences, the National Research Council, the journalistic profession, and the Scripps Estate have three representatives each on the board. The institution which has

played such an outstanding role in the popularization of science has also renamed the following officers: president, Harlow Shapley, director of Harvard College Observatory; vice-president and chairman of the Executive Committee, Alexander Wetmore, secretary of the Smithsonian Institution; treasurer, O. W. Riegel, director of the Lee School of Journalism, Washington and Lee University; and secretary, Watson Davis, director of Science Service. Additional members of the Executive Committee are Frank R. Ford, editor of the *Evansville* (Indiana) *Press*, and E. G. Conklin, of Princeton University.

A research conference on coccidiosis is being planned by the New York Academy of Sciences for March 3–4, 1949, at the American Museum of Natural History in New York City, and investigators in this field throughout the country will be invited to attend. The Organizing Committee is anxious to receive suggestions that will aid in making the conference an extremely successful one. Further details may be obtained from Sterling Brackett, Organizing Chairman, American Cyanamid Company, 1937 West Main Street, Stamford, Connecticut.

Officers of the Crystallographic Society of America, which recently met jointly with the American Society for X-ray and Electron Diffraction for the first time (*Science*, April 23, p. 419), are shown on this week's cover. They are, left to right: S. G. Gordon, Academy of Natural Sciences, Philadelphia, counselor; J. W. Gruner, University of Minnesota, retiring president; A. Pabst, University of California, president; and William Parrish, Philips Laboratories, secretary-treasurer.

The annual initiation ceremonies, reception, and banquet of the Kappa Chapter of Sigma Xi were held at the Men's Faculty Club, Columbia University, Tuesday evening, May 4. One hundred forty-eight new members were initiated. Irving Langmuir, 1932 Nobel Prize winner and associate director of General Electric Research Laboratories, gave the Sigma Xi address, "Weather, Its Causes and Relationships." The following officers of the Kappa Chapter were elected for 1948–49: president, Paul F. Kerr, professor of geology; vice-president, John M. Nelson, professor emeritus of chemistry; and secretary-treasurer, John S. Karling, professor of botany.

NRC News

A conference on conservation in Micronesia was held in Honolulu on April 19–20, under the auspices of the Pacific Science Board of the National Research Council. Edwin H. Bryan, Jr., the Board's Honolulu officer, reports that discussions centered around the conservation of renewable natural resources, and the preservation of unique and irreplaceable natural features, archaeological sites, and historical monuments.

Scientists familiar with Micronesian conditions and others with experience in conservation, representing several government departments as well as scientific institutions in Hawaii, were invited to attend. The Bernice P. Bishop Museum and the University of Hawaii were hosts to the conference, which was organized by F. R. Fosberg, a member of the University's botany faculty, in collaboration with the Honolulu office of the Pacific Science Board. Harold J. Coolidge, executive secretary of the Board, was in Honolulu for the occasion.

The results of this conference are to be used as the basis for a subsequent conference on the same subject to be held in Washington, D. C. The date of the latter has not been announced.

Deaths

Axel F. Enström, 73, a leader in the organization and promotion of Swedish technical research, died in Stockholm March 31. In 1919 he organized the Swedish Academy of Engineering Sciences, of which he was managing director until 1938 and president from 1938 to 1940. From 1922 to 1935 he was president of the Swedish Standards Commission.

Oscar W. Oestlund, 90, a member of the Department of Zoology, University of Minnesota, from 1885 until his retirement in 1927, died at his home April 16.

William Thomas Shaw, 75, emeritus professor of zoology at Fresno State College, died of a heart attack at his home in Fresno, California, on May 13. At the time of his death Dr. Shaw was completing an extensive manuscript on the Columbian ground squirrel and was about to leave for the Northwest to visit the site where Lewis and Clark were camped when they described the species.

On the day preceding publication of the first issue of the new *Scientific American* (May 11), Gerard Piel, editor and publisher of the new monthly magazine, presented to the New York Public Library the 103-year-old first volume of the former *Scientific American*. The 178 volumes which make up the entire run of the magazine which was founded in 1845 by Rufus Porter, an inventor, will be delivered to the library at a later date.

The idea of the new *Scientific American* was originated by Mr. Piel and Dennis Flanagan, both former science editors of *Life*, and Donald H. Miller, Jr. The uniquely illustrated first issue features articles bearing on sociology, anthropology, "social physics," medicine, astronomy, biology, physics, and the operation of blast furnaces. In addition, there is a section devoted to material of interest to the amateur astronomer, a book review department, a section describing recent developments of a governmental nature which affect every citizen, a letters to the editors department, and others. Both the layman who has an active interest in science and the scientist who considers himself a layman in fields other than his own will find among the pages of the new *Scientific American* material which is as diversified as it is readable.

An impressive memorial in bronze and granite, topped by a flagstaff and depicting the various services performed by pharmacists in the wars of our country, was dedicated on the grounds of the American Pharmaceutical Association in Washington, D. C., on May 7. The national memorial is the gift of H. A. B. Dunning, of Baltimore, past president and member of the Council of the Association. In connection with the dedication cere-

monies a series of conferences were held which were aimed at coordinating pharmacy manpower and services for efficient use in any future national emergency. In a session over which George D. Beal, chairman of the Association's Council presided, D. W. Bronk discussed the part played by the NRC in pharmaceutical science, and pharmacy in the military services was discussed by the Surgeons General of the Navy and Army and the Air Surgeon. S. H. Dretzka, president of the American Pharmaceutical Association, presided over another session which included papers on "Accomplishments of the National Health Assembly, by J. Donald Kingsley, Assistant Administrator of the Federal Security Agency; "The U. S. Public Health Service," by Surgeon General Leonard A. Scheele; "Medical Implications of Atomic Warfare," by Phillip S. Owen, executive director of the Committee on Atomic Casualties; "The National Blood Program of the American Red Cross," by the program's administrator, Ross T. McIntire; "The Selective Service," by Major General Lewis B. Hershey; and "The Council on National Emergency Medical Service," by Richard L. Meiling, secretary of the Council.

A committee of the Botanical Society of America, which is in process of gathering new and outstanding ideas for teaching aids for a general botany course, is soliciting the aid of high school and college teachers of general botany and general biology courses in the hope that they will be willing to share with others any particularly effective demonstration methods or techniques which they are using. Credit will be given to the sources of all ideas embodied in a report to be presented next September. The committee would particularly appreciate copies of local laboratory manuals and outlines of experiments not commonly used in currently published manuals. Suggestions should be mailed to Victor A. Greulach, Texas A & M College, College Station, Texas.

New low-temperature laboratories have recently been opened in the Division of Mechanical Engineering of the National Research Council of Canada. Until now, only very limited laboratory facilities for small-scale tests have been available in Canada, although advanced bases for field testing have been set up as far North as transportation conditions permitted. In the new laboratories there are three cold chambers, the largest of which can accommodate test specimens up to 50 feet in length by 15 feet in width. The refrigeration plant, one of the largest of its kind in Canada, enables temperatures as low as $-80°$ F to be obtained in all of the cold rooms and the achievement of a considerable drop or rise in temperature within a relatively brief period. J. L. Orr, a University of Toronto graduate in engineering physics, is in charge of the laboratories and will direct work on problems ranging from the development of suitable clothing for Arctic use to studies of cold-weather starting and running of engines.

Establishment of a Technical Development Committee on Upper Atmosphere and Interplanetary Navigation by the Institute of Navigation has just been announced by Rear Adm. G. G. McLintock, the Institute's president. Co-chairmen of the new committee are Paul Rosenberg, president of Paul Rosenberg Associates, of New York, and Samuel Herrick, professor of astronomy, University of California at Los Angeles, and the membership includes: A. G. McNish, chief of the Basic Ionosphere Research Section, National Bureau of Standards; Maj. R. A. Trenkle, First Experimental Guided Missiles Group, Eglin Field, Florida; John C. Bellamy, director, Cook Research Laboratories, Chicago; and Frederick Franklin, Oak Ridge Laboratories. The co-chairmen, in a statement issued last week, point out that advances in rocket engineering and the possibility of using atomic power for propulsion purposes "make it feasible to foresee the propulsion of an uninhabited projectile into space beyond the earth's atmosphere." For the time being, however, attention will be devoted to a study of the purely navigational aspects of interplanetary travel.

An up-to-date list of all national standards approved by the American Standards Association, published late last month, is now available free of charge from the Association's offices at 70 East 45th Street, New York City 17.

Rohrer, Hibler and Replogle, a firm which numbers approximately 30 full-time psychologists who are serving as psychological counsel to management in some 176 corporations in this country and the British Commonwealth, has recently announced the following changes with respect to its staff: J. Elliott Janney, formerly secretary of the firm, is now partner in charge of Research and Development, with offices at 520 Terminal Tower, Cleveland 13, Ohio. At the same address, Paul J. Brouwer has assumed the position of regional director, and Lynde C. Steckle, that of staff psychologist, while George Spache has been appointed staff psychologist in the New York Office. In addition to the home office in Chicago and the Cleveland and New York branches, the firm maintains branches in Dallas and Los Angeles.

Make Plans for—

National Gastroenterological Association, 13th annual convention, June 7–10, Hotel Pennsylvania, New York City.

American Neurological Association, June 14–16, Claridge Hotel, Atlantic City, New Jersey.

American Dairy Science Association, 43rd annual convention, June 14–16, University of Georgia, Athens.

American Society for Engineering Education, June 14–18, University of Texas, Austin.

Mycological Society of America, annual foray, June 15–17, Biological Station, University of Michigan, Cheboygan.

American College of Radiology, June 18–20, Continental Hotel, Chicago, Illinois.

American Mathematical Society, June 19, University of British Columbia, Vancouver.

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AAAS

Centennial Celebration

Washington, D. C.

September 13–17, 1948

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Comments and Communications

International Depot of Microscopic Preparations of Cytology

In 1939 the International Union of Biological Sciences requested Prof. P. Martens, director of the J. B. Carnoy Institute, Louvain, Belgium, to take up again the project of an International Depot of Microscopic Preparations of Cytology, animal and vegetable. This plan had previously been submitted by the Union to the late Prof. V. Gregoire, but owing to poor health he was unable to realize the practical side of this plan. Various circumstances have delayed until now the announcement of the creation of this organization.

Preparations obtained from numerous research centers which have already been used as a basis for previously published work will therefore be grouped together in an easily accessible center—the Laboratory of Cytology of the Carnoy Institute at Louvain, Belgium. Each worker interested in a definite problem may thus compare with his own documentation the original microscopic documentation of other authors relative to the same matter. It is hardly necessary to underline the considerable interest that a depot of this kind will acquire and, also, how much it will favor good understanding among workers and smooth out many difficulties and vain contestations which are inclined to permeate scientific literature.

This result can be obtained only with the greatest comprehension and collaboration of the greatest possible number of cytologists. The IUBS therefore invites them, from now on, to send their reprints to the Laboratory, enclosing with them preparations already used as a basis for published work, and to bring such deposits up to date in the future. It is desirable that the fields considered by authors as particularly demonstrative or used as published illustrations should be specially noted as clearly as possible on the preparations. It is also requested that a sample of the published work should be attached when these are sent.

Every biologist known for his publications, and any other person possessing authorized recommendation, will be able to consult and study as much as he likes all preparations which have been entrusted to the Depot; consultants will have the Laboratory and necessary optical instruments at their disposition. All work must be done within the Depot unless written permission to withdraw material is granted by the depositor.

The preparations will always remain the *property solely of the depositors,* who can at any time have them sent back to them. The cost of postage would then be paid by the administration of the Depot.

P. VAYSSIÈRE (Paris)
Secretary General, IUBS
P. MARTENS (Louvain)
Administrator of the Depot

On the Properties of Gelatin-Dye Phosphors and the Continuum Theory of Szent-Gyorgyi

In his recent book entitled *Chemistry of muscular contraction* (New York: Academic Press, 1947), Szent-Györgyi presents a theory and some preliminary experiments which attempt to relate luminescence phenomena of gelatin-dye phosphors with the fundamental mechanisms of energy exchange in biological systems. Although the present writer has no intention of quenching Szent-Györgyi's enthusiasm for this new approach, he is inclined to make a few criticisms of the theory. This seems necessary, since the "Continuum Theory" has already been heralded as an important new principle in theoretical biology by one reviewer, whereas the phenomena on which it is based seem to have a simpler and more tangible interpretation in terms of spectroscopic research on the luminescence of complex molecules.

Szent-Györgyi's basic premise is that the electronic transitions involved in the luminescence of gelatin-dye phosphors are closely related in character to the electronic processes in mineral "impurity" phosphors. He regards the dye as taking the role of the impurity, and the luminescence as a property of the system rather than of the dye or the gelatin. He then attempts to deduce the electronic energy levels of a protein as a "fusion" of the spectroscopic terms of the component atoms.

A careful study of the experiments described and the interpretations presented indicates that the latter are in direct conflict with theoretically secure ideas previously established to account for such phenomena. The interpretations of complex molecule luminescences made here by the late G. N. Lewis and his co-workers have been along the lines of straightforward π-electron spectroscopy. The phenomena observed by Szent-Györgyi and his associates appear to be due simply to the optical properties of the dye molecules. Most of the experiments reported may be interpreted in terms of the general theory of luminescence of complex molecules; this theory has been reviewed and expanded in a recent paper by the present writer (*Chem. Rev.*, 1947, 41, 401).

In his discussion, Szent-Györgyi does not distinguish between fluorescence and phosphorescence, using the terms interchangeably. It is noteworthy that in several cases reported by him the appearance or disappearance of luminescence coincides with an increase or decrease in the viscosity of the system, respectively. It is suggested that a careful spectroscopic study of the phosphorescence spectra of adsorbed dyes and of the same dyes in rigid glassy media (*Chem. Rev.*, 1947, 41, 401) would clear up many of the ambiguities. This would require careful attention to purity of the sample, to possible photochemical changes induced by the exciting light, and resolution of the fluorescence and phosphorescence spectra by means of a phosphoroscope.

In discussing the photoconductivity experiments of Boros, Szent-Györgyi does not include a description of the light source used, and while it may be assumed to have been considered, it cannot be ascertained from the presentation whether the differential absorption of the

various dyes was taken into account. The possibility of photochemical changes was not checked. The results of these difficult experiments on photoconductivity are easily vitiated by small disturbances.

The electronic systems of proteins may very well be unique and deserve careful study, but it is first necessary to demonstrate that the phenomena observed may not be interpreted on the basis of appropriate extant theories. In the present case, it seems more reasonable to apply principles established for the electronic energy levels of complex molecules rather than for the energy levels of the metallic or crystal lattice.

MICHAEL KASHA

University of California, Berkeley

Water at −72°

Dr. Earl C McCracken recently reported (*Science*, November 7, 1947, p. 453) some interesting examples of water undercooled to −10° which he observed accidentally when testing home freezers. A systematic investigation of the causes and conditions of undercooling, which may partly explain Dr. McCracken's observations, was undertaken a few years ago in Germany by Dr. Walter Rau in the laboratory of Prof. Erich Regener (*Schriften der deutschen Akademie fuér Luftfahrtforschung*, 1944, Vol. 8, Pt. 2). This proved that it is possible, by adequate treatment, to keep water liquid as far down as −72°.

Dr. Rau came to the following conclusions: Freezing is initiated by "freezing nuclei," foreign particles, just as condensation of water into clouds is initiated by condensation nuclei. Not all these nuclei respond at the same temperature. Only a few are active at zero; most of them, between 10° and 12°. If the nuclei are kept resting for a long time in water or in moist air, they lose their activity but regain it by drying. If an individual drop is allowed to freeze and melt again repeatedly, it will first freeze several times at the same temperature, but then it suddenly drops to a lower temperature before refreezing. In this way the freezing could be gradually driven down to −72°.

When the water solidified at this low temperature, it crystallized around "germs"—that is, the smallest accumulation of the molecules of the new phase, without the assistance of foreign bodies; in this case the ice no longer appeared in the well-known hexagonal crystals, but in a new modification, forming cubes, octahedrons, or tetrahedrons.

GABRIELE RABEL

49 Lensfield Road, Cambridge, England

Surface Tension and Conductivity of Penicillin Salts

Hauser, Phillips, and Phillips (*Science*, December 19, 1947, p. 616) recently reported that solutions of sodium penicillin are highly capillary active and concluded that sodium penicillin in water exists as a colloidal sol and not as a true solution. They obtained a surface tension of 31.7 dynes/cm for a solution containing 10,000 units of penicillin sodium salt (Abbott)/cc. On the other hand, Woodbury and Rosenblum (*J. biol. Chem.*, 1947, 171, 447) report from conductivity measurements that sodium penicillin in water behaves as a normal, completely dissociated electrolyte. These two findings are difficult to reconcile unless the measurements were made at widely different concentrations. This, however, is not the case. The concentration of 10,000 units/cc used in the surface tension measurements corresponds to 0.6% or to 0.017 moles/liter, which falls about in the middle of the range, 0.0007–0.0477 moles/liter, employed in the conductivity measurements.

We have carried out surface tension measurements on crystalline sodium penicillin G (Cutter Lot HB–88; potency, 1,600 μ/mg) and crystalline potassium penicillin G (Cutter Special Lot; potency, 1,570 μ/mg), using the du Noüy Precision Tensiometer and the capillary rise method. The results given in Table 1 show that these solutions have surface tensions differing but little from

TABLE 1

Solution	Surface tension Dynes /cm	Conc. (%)	Temp.	Method
Sodium penicillin G	70.8	0.6	23°	du Noüy Tensiometer
Water	71.1		23°	" " "
Sodium penicillin G	70.3	0.6	21°	Capillary rise
Potassium penicillin G	68.7	0.6	19°	du Noüy Tensiometer
Water	73.2		19°	" " "
Potassium penicillin G	70.1	0.5	21°	Capillary rise

that of pure water. The solutions therefore are not capillary active and behave as true solutions, not as colloidal sols.

Conductivity measurements carried out on crystalline potassium penicillin G gave a Λ_o value of 99.5 at 25°. A Λ_o value of 77.8 at 30° for sodium penicillin G was obtained by extrapolating Woodbury and Rosenblum's data to zero concentration. Taking into account the difference in ionic conductance between Na^+ (50.1 at 25°) and K^+ (73.5 at 25°), a value of 76.1 is obtained for the conductance of sodium penicillin G at 25° from our data on potassium penicillin. This is in good agreement with the above value of 77.8 at 30°. Thus, the conductivity measurements on potassium penicillin G are in agreement with those made on sodium penicillin G by other workers (*J. biol. Chem.*, 1947, 171, 447), and both these and our surface tension measurements indicate that sodium and potassium penicillin salts in water behave as true solutions and not as colloidal electrolytes.

We wish to thank the Cutter Laboratories for a grant and Profs. T. C. Daniels and Frank M. Goyan for helpful discussions.

W. D. KUMLER and EDWARD L. ALPEN

College of Pharmacy,
University of California, San Francisco

TECHNICAL PAPERS

Pulmonary Edema in Leucemic Mice Following Treatment With Urethane

WILLIAM W. WINCHESTER and GEORGE M. HIGGINS

Division of Experimental Medicine, Mayo Foundation, Rochester, Minnesota

In view of the recent report by Webster (*7*) regarding the toxic potentialities of urethane in the treatment of leucemia, it was felt desirable to present a preliminary report of some of the toxic manifestations noted in a study of urethane and its effect on transplanted leucemia in the mouse.

Until recently, urethane has been described as non-toxic when used in therapeutic doses (*1*) (adult hypnotic dose: 2–4 gm). Because of its feebly hypnotic effect on adult human beings, it was seldom used except as an anesthetic agent for laboratory animals, with the result that few observations on the extended use of urethane in man are available. Certain isolated effects in laboratory animals and in human beings have been reported, however, among them being capillary changes, which are the chief concern of this paper.

Sollmann (*6*) in 1917 reported the formation of wheals when urethane was applied to scarified skin. Krogh and Harrop (*3*) in 1921 described the effects of local applications of 5 and 25% solutions of urethane on capillaries of the frog's tongue. Dilatation and increased permeability were noted, progressing to a stage they called "stasis"—a condition of increased concentration of the blood corpuscles due to rapid loss of plasma. The increased viscosity of such blood caused the flow to be sluggish and finally to cease as the venous capillaries became filled with plugs of tightly packed corpuscles. Krogh and Harrop expressed the belief that the effects were due primarily to capillary dilatation.

Landis (*4*) in 1927, using a micropipette technic, perfused mesenteric capillaries of the frog with dilute solutions of urethane and observed changes in capillary permeability similar to those noted by Krogh and Harrop. He expressed the opinion, however, that this resulted from a direct toxic effect of the urethane on the endothelium and from increased capillary pressure due to blockage of venous capillaries.

Kirschbaum and Bell (*2*) in 1947 reported the induction of glomerular lesions by urethane in mice of the NH strain, a strain in which spontaneous glomerulonephritis develops. In this instance the glomerular capillaries especially seem to be susceptible to the effects of urethane.

We have not encountered in the literature any reference to the state of pulmonary capillaries of experimental animals following urethane anesthesia. However, Moon and Morgan (*5*) in 1936 studied the lungs of dogs in which a state of both continuous and intermittent narcosis by sodium phenobarbital was induced. They likewise found evidence of increased capillary permeability. This progressed to marked pulmonary edema, leading to shock and death in the most severe forms, bronchopneumonia in the less severe, and recovery when edema was very mild.

In our experiments, the effect of urethane on transplanted myelogenous leucemia produced in F–NH hybrid mice was studied. Three groups of mice previously inoculated with suspensions of a leucemic spleen were selected for study when their leucocyte counts had arisen to the neighborhood of 200,000 cells/mm³ of blood. Urethane was administered intraperitoneally to the first group in daily doses of 0.5 mg/gm of body weight. It was administered similarly to the second group at a level of 1.0 mg/gm of body weight. The third group was divided into three subgroups. Subgroup A received 0.75 mg/gm of body weight daily; subgroup B, 1.0 mg/gm every second day; and subgroup C, 1.0 mg/gm every third day.

TABLE 1

DATA ON TREATMENT OF LEUCEMIC MICE WITH URETHANE

Strain of mice	Medication	Dose/gm of body weight*	Percentage incidence		Average weight of lungs (mg)
			Edema	Hydrothorax	
Normal C	Physiologic saline	0.01 cc daily	0.0	Not recorded	140.6
Normal C	Urethane	1.0 mg daily	100.0	Not recorded	384.6
Leucemic F–NH	Physiologic saline	0.01 cc daily	0.0	0.0	237.5
" "	Urethane	0.75 mg daily	100.0	73.7	394.1
" "	"	1.0 mg every second day	81.8	41.6	392.7
" "	"	1.0 mg every third day	83.3	25.0	339.1

* The anesthetizing dose of urethane in the mouse is generally considered to be 1 mg/gm of body weight.

Injections and observations were continued until death of the animal or until the approach of the moribund state, when animals were killed for study.

In addition, urethane was administered daily to normal C strain mice in amounts similar to those given to the second group of leucemic mice.

Among other criteria of the effectiveness of the drug, the life span of each animal was of considerable importance. This measurement was markedly affected in the first series of mice by the development of pneumonia in three-fourths of the treated animals. It was not realized until the pathologic sections were studied that this pneumonia was superimposed on, and probably was secondary to, a relatively mild pulmonary edema, which was present in all the treated animals. In the second series, which received the largest amount of urethane, the life span was also reduced by the development of pulmonary edema of a more severe and more rapidly fatal variety in all of the animals. This occurred not only in the leucemic but also in the normal C strain animals receiving similar doses of urethane. In the third series of animals, graded doses of urethane were used in an effort to attain control of the leucemia without the development of pulmonary edema. Doses sufficiently large to result in a reduction of the total leucocyte count with a shift to the right and a reduction in the sizes of the liver, spleen, and lymph nodes caused pulmonary edema in all of the cases. The smaller doses of urethane were ineffectual in maintaining an initially favorable response, and even these ineffective amounts resulted in the development of pulmonary edema of lesser degree in many of the animals. In this latter group, death resulted, if not immediately from the edema, several days later from pneumonia. Other evidences of capillary damage throughout the body were seen grossly in a large percentage of these cases.

At necropsy, animals with pulmonary edema frequently showed the customary accumulations of pinkish-brown, frothy material about the nares and mouth. On opening the thorax, fluid, usually of a serosanguineous nature, was frequently encountered. The lungs were always tense, completely filling the thorax. Their appearance varied from a pinkish-brown, almost translucent character to a mottled bright and deep red. Petechiae were often seen. On section of the trachea, as well as of the lung parenchyma, large quantities of fluid exuded, after which the lung became quite compressible. Microscopically, the alveoli and the bronchi were distended and filled with a pink-staining homogeneous material. There was marked capillary engorgement with evidence of rupture and release of erythrocytes into the alveoli. Areas of bronchopneumonia were present in animals in which the pulmonary edema was less severe and not immediately fatal.

Although edema in these animals was almost entirely confined to the lungs, other evidences of capillary damage were noted. The axillary and inguinal regions were, in nearly all cases, sites of subcutaneous petechiae and frequently of localized anasarca. The site of intraperitoneal injection (constant because of anatomic reasons) often revealed subcutaneous petechiae progressing at times to ecchymoses. From the low incidence in the untreated controls it may be assumed that these phenomena are not due solely to thrombocytopenia secondary to leucemia. The comparative gross data relative to the foregoing observations are presented in Table 1.

Although we realize that observations on laboratory animals can seldom be applied directly to man, it is the aim of this paper to increase the awareness of the toxic potentialities of urethane, when used over a period of time, particularly with respect to capillary damage.

References

1. Goodman, L. S., and Gilman, Alfred. *The pharmacological basic of therapeutics.* New York: Macmillan, 1941.
2. Kirschbaum, Arthur, and Bell, E. T. *Proc. Soc. exp. Biol. Med.*, 1947, **64**, 71–72.
3. Krogh, A., and Harrop, G. A. *J. Physiol.*, 1921, **54**, cxxv–cxxvi.
4. Landis, E. M. *Amer. J. Physiol.*, 1927, **81**, 124–142.
5. Moon, V. H., and Morgan, D. R. *Arch. Path.*, 1936, **21**, 565–577.
6. Sollmann, Torald. *J. Pharm. exp. Therap.*, 1917, **9**, 391–392.
7. Webster, J. J. *J.A.M.A.*, 1947, **135**, 901–903.

Use of Radioactive Diiodofluorescein in the Diagnosis and Localization of Brain Tumors[1]

George E. Moore[2]

Department of Surgery,
University of Minnesota Medical School, Minneapolis

The use of fluorescein has recently been suggested as an aid in the diagnosis of malignancy (*1*). In the initial report it was observed that brain tumors appeared to exhibit a consistent special affinity for the absorption of previously injected fluorescein.

In an attempt to extend the clinical usefulness of the fluorescein technique, radioactive derivatives of the dye have been prepared. Since it is considered safe to use, for clinical purposes, only those isotopes with a short half-life, and since the detection of deep-seated intracranial lesions requires the emission of gamma radiation, diiodofluorescein was synthesized to contain I^{131}. The amount of I^{131} added was adjusted to give 1 mc of radioactivity/10 cc of a 2% solution of the final product, sodium diiodofluorescein. An amount of dye calculated to contain 500–600 μc of radioactivity was injected intravenously in each case. In order to give a comparable dose of radioactivity to patients on subsequent days,

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[2] Senior Research Fellow, U. S. Public Health Service.

increasing volumes of the dye were injected as the I^{131} decayed. Previous toxicity studies have shown that the ML/50 of diiodofluorescein is comparable to that of eosin; no toxic reactions have been encountered from the small amount of dye administered.

All counts were obtained by means of a beta-gamma Geiger-Müller tube protected from background radiation by a 2-cm-thick lead shield, provided with a lead cone to reduce the area being counted, and mounted on a portable X-ray unit. Thin lead foils were placed over the counter window to filter out beta radiation. A quenching circuit attached directly to the Geiger-Müller tube from the scaler allowed easy manipulation of the detection unit over the patient. Counts were taken for 3- to 5-min intervals at each of several positions on the skull with the cone of the detection unit directly on the skin. An attempt was made to obtain counts over symmetrical positions on the right and left sides of the head, as well as counts along the midline. After a complete survey, an examination of sites of higher activity was repeated in order to localize more definitely the suspected lesion. At times uncooperativeness of a patient due to the intracranial lesion made an adequate survey impossible.

Although counting was begun soon after dye was injected, differential readings between areas over the suspected tumor and symmetrical control areas did not become evident until an interval of 2–4 hrs had elapsed. This interval, required for the development of maximal differences in concentration of dye by the normal and tumor tissue, corresponds closely to the time lag prior to the appearance of maximal fluorescence noted in the earlier study (*1*) of brain tumors. Soon after the dye is injected, higher counts are obtained over the large venous sinuses; then, as the dye is removed from the blood stream, the counts tend to equalize over all parts of the brain with the exception of the area over the tumor, where the highest counts are recorded. In cases in which the tumor is accompanied by a large amount of edema, somewhat higher counts may be obtained over the entire affected hemisphere. As experience with the technique increased, a single series of counts at the proper interval was found satisfactory to localize the tumor. A majority of the tests were carried out without knowledge of the neurological findings, roentgen examination, and staff opinion. Only cases with questionable intracranial neoplasms were examined by this method.

To date 15 patients suspected of harboring intracranial neoplasms have been subjected to this technique. The last 12 cases are summarized in Table 1. Three previous cases with known site of recurrence, following previous partial operative excision, were studied by the radioactive dye method before the diagnosis of new cases was attempted.

TABLE 1

		Clinical preoperative diagnosis	Conclusions from radioactive dye technique	Operative findings
(1)	K.W.	Meningeoma of right sphenoid ridge	No tumor	Aneurysm of right internal carotid
(2)	E.S.	(?)Tumor of right temporal or parietal lobe	Tumor of right parietal occipital area	Ependymal blastoma, right occipital lobe
(3)	T.B.	Tumor of right temporal lobe	(?)Tumor of right temporal area	Meningeoma of right middle fossa
(4)	P.K.	Metastatic tumor of right parietal lobe	Tumor in right parietal area	Metastatic tumor of right parietal lobe
(5)	L.S.	(?)Metastatic tumor of right motor cortex	No tumor on right; (?) tumor of left frontal lobe	No tumor on right, left side not explored
(6)	H.L.	(?)Tumor	Tumor of posterior frontal lobe on right	Glioblastoma of right temporal lobe
(7)	J.H.	Tumor of right frontal lobe	Tumor of right frontal lobe	Ependymal blastoma of right frontal lobe
(8)	J.B.	(?)Tumor	Tumor to left of the midline, posterior frontal area	Meningeoma of left posterior frontal area
(9)	G.H.	(?)Tumor	No tumor	Normal ventriculogram, no operation
(10)	E.J.	Large tumor of right parietal lobe	Tumor of right parietal area	Right parietal tumor by ventriculogram and biopsy
(11)	L.W.	Right acoustic neuroma	No significant counts	Right acoustic neuroma
(12)	A.B.	Subdural hematoma, right side	Tumor of right frontal lobe near midline	Meningeoma of right frontal lobe near midline

Correct diagnoses of negative findings (Cases 1 and 9), as well as positive, have been made. Case 12 is of special interest. From the results of the counts obtained with the radioactive dye technique, a definite area was outlined on the skull over the site of the tumor. This outline coincided closely to the extent of the superficially situated meningeoma found at operation.

The limitations of this technique are as yet unknown and its clinical usefulness is still to be determined. Further studies of the differential concentration of the radioactive dye in normal and edematous brain tissue as well as various tumors, clinical and experimental, are in progress. Preliminary experiments utilizing induced brain tumors in mice have revealed the concentration of dye in the tumor tissue to be as high as 80 times that found in the adjacent normal brain. Measurements of various concentrations of radioactive diiodofluorescein

under physical conditions simulating those found clinically have verified the feasibility of the technique and will be reported upon later.

Reference

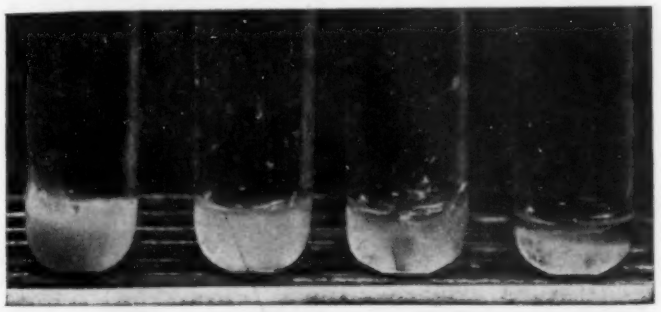
1. MOORE, G. E. *Science*, 1947, **106**, 130–131.

Similarity to Heparin of the Clotting Inhibitor in Acute Leucemia and the Significance of Hyperheparinemia in Estrapenic Cholinergic States

ROBERT D. BARNARD

Terrace Heights Hospital, Hollis, Long Island[1]

Heparin, the antithrombin of normal blood (*6*), is reported to be increased in instances of human pernicious anemia and leucoses (*2, 9*), in anaphylactic and peptone shock (*7*), and, more recently, in radiation morbidity in dogs (*1*). The basis for its identification in these conditions has been neutralization of thrombin (*2, 9*) or neutralization by globin (*2*) or by toluidine blue (*1*).



A B C D

FIG. 1. Human plasma clots formed by addition of Russell viper venom and calcium chloride to normal citrated plasma: A, normal clot; B, clot formed in presence of 1 mg% of heparin; C, 2 mg% of heparin; D, after dilution with an equal volume of plasma from a patient with terminal hemorrhagic acute leucemia.

Additional evidence for the heparin identity of the antithrombin in 5 patients with acute leucosis and 2 with thrombotic cardiogenic shock has been secured. Addition of the plasmas of these patients to citrated normal human plasma caused a dissociation in the precipitation rates of filiar and gelatinous fibrin when the plasma was clotted by calcium chloride-viper venom. In untreated citrated human plasma, the opaque filiar fibrin component (which appears to be precipitated through direct thromboplastin-fibrinogen interaction and is responsible for clot retraction, *4*) precipitates immediately prior to the formation of gelatinous fibrin (resulting from thrombin-fibrinogen interaction, the nonretractile, fibrinolyzable component), so that both components are disseminated uniformly throughout the body of the resulting opaque clot (Fig. 1A). In the presence of 1 mg% of heparin, gelatinization is delayed until retraction of the filiar fibrin has begun, so that both components of the clot can be separately distinguished (Fig. 1B). Dissociation is usually completed by the presence of 2 mg% of heparin (Fig. 1C). Fig. 1D shows the degree of dissociation produced by an added equal volume of the incoagulant plasma from a patient in the hemorrhagic phase of acute myeloblastosis, which indicates for this plasma a heparin content of between 2 and 3 mg%. Confirmation of this approximate figure for the heparin content of this patient's blood was secured by thrombin titration.

Hyperheparinemia of this extent, while explaining incoagulability, cannot, in itself, condition the hemorrhagic diathesis. Equal or greater heparin concentrations are frequently attained, temporarily at least, in human blood, since it is now common clinical practice in the treatment of thrombophlebitis to administer 100 mg of heparin by single intravenous injections. During dicumerol therapy, occasional patients who exhibit a spontaneous autochthonous hyperheparinemia have been encountered without relationship to any tendency to capillary bleeding.

Attention has been directed to the apparent limitation of hyperheparinemic extravasation to the estrapenic conditions, those characterized or attended by a diminution in the blood cholinesterase concentration (*5*). Estrapenia, per se, might explain hyperheparinemic extravasation on the basis of cholinergic capillary paresis, but the possible interrelationships of estrapenia and hyperheparinemia have not hitherto been clarified. By the citation of some additional facts, their corollaries and elaborations, it may now be justifiable to attempt an explanation of the mechanism of hyperheparinemia arising during the estrapenic dyscrasias.

(1) The administration of heparin to a subject with normal hemopoietic function is followed, after the usual period of diminished blood coagulability, by a hypercoagulability state. This is familiar to clinicians as the "heparin rebound," which may occur if too long an interval is allowed between successive heparin administrations in the treatment of thrombophlebitis and by which the condition may actually be aggravated. Heparin hypercoagulability may also be demonstrated in the rabbit and the dog; in the latter animal the writer has seen coagulation times of 20–30 *sec*, 4 hrs after administration of coagulation-abolishing doses of heparin.

(2) During heparin rebound, the thromboplastin concentration of the blood is markedly increased, while in the hemorrhagic phase of estrapenic hyperheparinemia it is considerably diminished (*3*). In the thrombopenic forms of the acute malignant hematologic dyscrasias, even where coagulation time is apparently normal, the filiar fibrin component of the clot and clot retraction may both be absent. Since thromboplastin enters directly into the formation of the retractile filiar fibrin (*3*), thromboplastin deficiency in these states is further indicated.

(3) The elaboration of the major fraction, at least, of the blood (erythrocytic) cholinesterase is a hemopoietic marrow function (*8*). This is likewise true of the elaboration of the major fraction, at least, of the

[1] The observations recorded were made at Halloran General Hospital, Staten Island, prior to its closing as an Army installation. The kind cooperation and sponsorship of Maj. Helmuth Sprinz, Chief of Laboratory Service, is gratefully acknowledged.

blood thromboplastin (the thrombocytic). Estrapenia connotes a depression of the hemopoietic marrow, which is usually inclusive; not only erythropoiesis but mature granulopoiesis and thrombopoiesis are concomitantly depressed. Thromboplastin deficiency may be related to the estrapenia only in the sense that the latter usually signifies panmyelophthisis, the marrow being unable to elaborate thromboplastin because it can elaborate few, if any, of its peripheropetal products.

If in light of the foregoing points the further assumption be permitted that heparin is the agent that evokes and regulates the rate and extent of thromboplastin production by the hemopoietic marrow (heparin having, in turn, its own antithrombic activity curtailed by the elaborate), there is forthcoming an explanation not only of the dynamic equilibrium maintaining normal intravascular fluidity but also one of the origin of hyperheparinemia in marrow failure. The blood heparin concentration will rise when blood thromboplastin is not available for its neutralization, a situation extant in the myelophthises. The teleologic possibility that heparinemia is augmented under these circumstances by cholinergic activation of mast cell function remains to be explored.

Addendum: The actuality of cholinergic mast cell proliferation has been indicated by the recent finding of coincident basophilic myelocytosis, absolute hyperheparinemia, and estrapenia in three patients with purpura (*3*).

References

1. Allen, J. G., and Jacobson, L. O. Science, 1947, **105**,
2. Barnard, R. D. *Urol. cutan. Rev.*, 1947, **51**, 46.
3. Barnard, R. D. Unpublished data.
4. Barnard, R. D., and Rein, C. R. *J. lab. clin. Med.*, 1944, **29**, 1287.
5. Mackowiak, E. J., and Barnard, R. D. *J. Amer. pharm. Ass.*, 1947, **36**, 383.
6. Quick, A. J. *Amer. J. Physiol.*, 1938, **123**, 712.
7. Quick, A. J. *The hemorrhagic diseases*. Springfield, Ill: Charles C. Thomas, 1942.
8. Sabine, J. C. *J. clin. Invest.*, 1940, **19**, 833.
9. Volkert, M., and Hertel, E. *Ugesk. Laeger*, 1943, **105**, **781.**

Use of a Plastic Material to Increase the Action of the Sodium Salt of 2,4-D[1]

C. L. Hamner and Kiang Chi-Kien

Department of Horticulture, Michigan State College

The effect of various compounds in increasing the action of the sodium salt of 2,4-D has been reported (*1*, *2*). It was demonstrated that the herbicidal action of the sodium salt of 2,4-D can be greatly increased either by acidification of the solution or by the use of certain onion extracts in combination with 2,4-D.

Materials or methods which are able to modify the action of 2,4-D may provide additional clues to explain the mechanism of metabolic processes in plants. This paper reports some very striking effects produced on bean plants when the sodium salt of 2,4-D was combined with a plastic material formulated from polyvinyl chloride, which is nontoxic to plants and is called Geon 31X latex[2].

Experiment I. Seeds of red kidney bean, selected for uniformity, were planted in 4″ pots in the greenhouse. Each pot contained two plants that were treated when the first trifoliate leaf was expanding. Ten pots were used for each treatment.

Application of 2,4-D was made by dipping one of the primary leaves of each treated plant into solutions containing the sodium salt of 2,4-D in varying concentrations of 0, 5, 50, 250, and 500 ppm. After the solutions had dried, the treated leaves of half of the plants were sprayed with a dispersion of 5% Geon 31X latex.

Within 48 hrs after treatment, marked differences were noted between the plastic- and nonplastic-treated lots. Curvature of the first internode and epinasty of the leaves were much more pronounced in the plants which had received a plastic coating in addition to the 2,4-D treatment. Nine days after treatment, all the plants that had been treated with 500 ppm of 2,4-D were dead. In the group treated with 250 ppm, death occurred in all the plants which had received, in addition to the 2,4-D, the 5% plastic coating. Those plants that received only 2,4-D were beginning to resume new growth. Although the stems were swollen and the leaves and petioles somewhat twisted, the plants were definitely recovering from the treatment (Fig. 1). In the group treated with 50 ppm of 2,4-D, only those plants that had received, in addition, a 5% spray of Geon 31X latex were severely affected; some of the plants were dead, and those not killed by the treatment showed no new growth and no sign of recovery. Where 5 ppm of 2,4-D was used, the addition of the plastic did not increase the response of the plants.

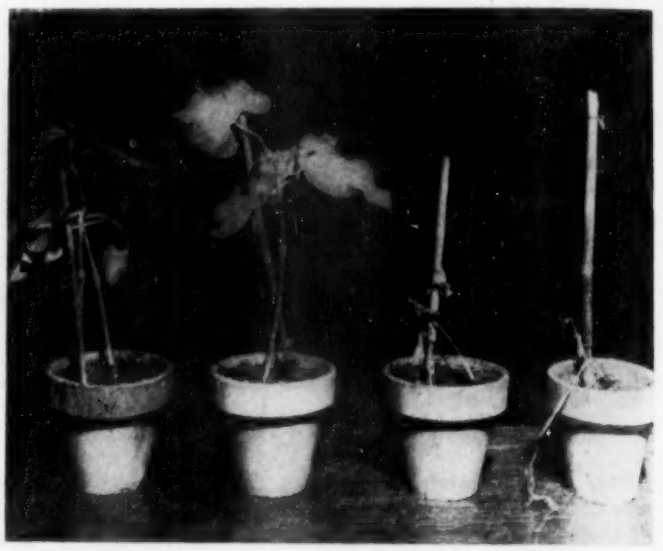


Fig. 1. Effect of Geon 31X in increasing the action of 2,4-D. Plants on the left were treated with 250 ppm of 2,4-D salt by dipping one of the primary leaves in the solution of 2,4-D. Plants on the right received the same concentration of 2,4-D, but, in addition, the treated leaves were sprayed with 5% of Geon 31X plastic.

[1] Journal Article No. 958 (n.s.) of the Michigan Agricultural Experiment Station.

[2] The material was obtained through the courtesy of the B. F. Goodrich Chemical Company, Cleveland, Ohio.

Experiment II. In this experiment the plastic material was added directly to the solution of 2,4-D. Ten-day-old red kidney bean plants were used as the experimental material, and applications were made by placing a single drop of the solution on the base of one of the primary leaf blades. Pipettes which released 0.05 ml of solution were used for applying the drops. The amount of 2,4-D used in all the solutions remained constant at 1,000 ppm; the amount of plastic material added to the 2,4-D, however, ranged from 0% to 1, 5, and 10%. The plants were harvested 2 weeks after treatment, and the average fresh weight of growth above the primary leaves was recorded for each treatment.

Differences between treatments were noted a few hours after application. It was evident that the response of the bean plants was directly proportional to the concentration of the plastic in the solution. The plants treated with 2,4-D plus a 10% concentration of the plastic showed the greatest degree of inhibition. Those treated with 2,4-D and a 1% concentration of the plastic, although not so severely inhibited as those with the 10% plastic, were nonetheless much more affected than were those receiving only 2,4-D (Table 1). No inhibiting effect was noticed

TABLE 1

FRESH WEIGHT OF BEAN SHOOTS DETERMINED 14 DAYS AFTER TREATMENT WITH 2,4-D SALT AND GEON 31X LATEX*

Treatment (2,4-D at 1,000 ppm)	Average weight of shoot/plant (gm)	Average weight of shoots on per cent basis 2,4-D = 100
Control (untreated)	2.45	144
2,4-D salt	1.70	100
" " + 1% Geon 31X latex ..	.39	23
" " + 5% " " " ..	.25	14
" " + 10% " " " ..	.23	13

*The weights represent all growth above the primary leaves.

when the entire plant was sprayed only with the Geon 31X latex in concentrations of 1, 5, and 10%.

Experiment III. Since the addition of Geon 31X to a 2,4-D salt solution increased the action of 2,4-D, an experiment was devised to test this combination upon a monocotyledonous plant which ordinarily would be resistant to 2,4-D.

Young oat seedlings approximately 4″ tall were treated with sprays containing 1,000 and 3,000 ppm of 2,4-D. In addition to 2,4-D, some of the sprays contained Geon 31X at 6, 12, and 25%. Plants treated with 2,4-D solutions alone showed no visible effect. Those treated with 2,4-D at 3,000 ppm together with Geon 31X at 25% were severely injured, and almost all the plants died. Plants treated with 2,4-D at 1,000 ppm together with Geon 31X at 25% were also injured, but not as severely; a few of these plants died. Plants treated with 2,4-D at 1,000 and 3,000 ppm together with Geon 31X at 6% were not injured.

The results indicate quite clearly that when Geon 31X latex, a water-dispersible, nontoxic plastic material, is added to 2,4-D either directly in solution or as a coating over plants previously treated with 2,4-D, the effect of the 2,4-D is greatly increased.

The manner in which the plastic material acts to increase the effectiveness of 2,4-D is not known. It is quite possible, however, that the plastic material, which has a low moisture vapor transmission coefficient may seal in the vapors of 2,4-D and hence increase its action because of a more intimate contact with the vapors. It is also possible that the carbon dioxide and oxygen relationships are changed as a result of the coating and hence affect the physiology of the cells, making them more susceptible to 2,4-D injury. The plastic coating may also increase moisture on the cell surface beneath the coating, thus permitting better penetration of the 2,4-D into the plant.

References

1. HAMNER, C. L., LUCAS, E. H., and SELL, HAROLD M. *Mich. agric. exp. Sta. Quart. Bull.*, 1947, **29**, 337–342.
2. LUCAS, E. H., and HAMNER, C. L. *Mich. agric. exp. Sta. Quart. Bull.*, 1947, **29**, 256–262.

Application of Chromatography to Segregation Studies of the Agent of Chicken Tumor I (Rous Sarcoma Virus)[1]

VERNON T. RILEY

National Cancer Institute, National Institute of Health, Bethesda, Maryland

Separation of the virus-like agent of chicken tumor I from the morphologically similar normal constituents of the extract has been attempted by various methods, including flask adsorption, chemical precipitation, selective extraction, and differential centrifugation. The differences in behavior of the tumor agent and some of the nonvirus substances of the extract in the various purification techniques employed was, however, so slight as to make complete separation difficult (*1, 4, 6, 7*).

The achievements of chromatography in the separation of closely related chemical substances (*8, 9*) suggested an exploration of the applicability of the method to the problem of separating morphologically similar subcellular particulates.

Exploratory experiments had indicated that the tumor agent was strongly, but reversibly, adsorbed on diatomaceous silicon dioxide (Celite) in the presence of physiological concentrations of sodium chloride. This combination of relatively inert substances provided the basis for a nondenaturating chromatographic system.

A partially purified chicken tumor extract (*4*) was prepared in 0.9% saline (−0.8 log molar), and equal quantities (50 ml) were adsorbed on identical micro-columns, 8 × 35 mm, consisting of 0.5 gm of Celite as adsorbent.

Seven columns containing the adsorbed agent were developed with 10 ml of 0.9% saline, and each was then eluted with 10 ml of a sodium chloride solution ranging in log molarity from −2 through −5 and terminating

[1] A detailed report will appear in an early issue of the *Journal of the National Cancer Institute.*

with distilled water. The eluate from each column was analyzed for nitrogen and tested in a balanced quantitative bioassay for tumor agent (*2*, *3*).

The data summarized in Table 1 and Fig. 1[2] demonstrate the influence of salt concentration in effecting the degree of adsorption or elution of the agent on the silica column. The following experiment was undertaken to determine whether the agent exhibits typical chromatographic banding characteristics:

Ten gm of Celite, deposited from a distilled water suspension, were employed to yield a column 34 × 42.5 mm. A total of 100 ml of partially purified tumor agent extract in 0.9% saline was adsorbed on the column, followed by development with an additional 50 ml of saline. The solid adsorbent column was extruded and sectioned as indicated in Fig. 2. Each segment was suspended in distilled water and poured onto a Whatman No. 1 filter disk in a small Buchner funnel and eluted with 50 ml of cold distilled water. These eluates were tested for nitrogen and tumor agent concentration. The results are indicated in Fig. 2, which shows the relative quantity of agent and nitrogen eluted from each segment. The 50 ml of eluant from the top zone contained a virus concentration of 52% of the starting extract and 8.1% of the nitrogen. In this figure all fractions are compared to the top segment as 100%.

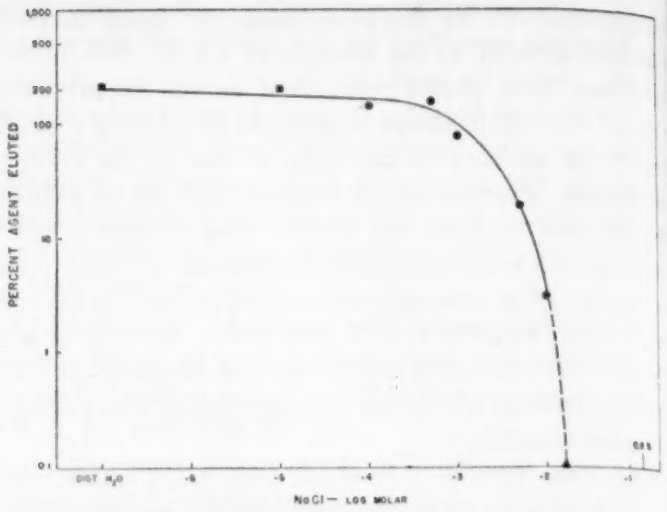


FIG. 1. Elution curve for the chicken tumor agent in the silica-saline chromatographic system.

The data of Table 1 and Fig. 1 contain several implications of biologic and chromatographic interest. In Fig. 1 it is seen that the eluants containing less than 0.001 molar salt concentration release more agent per unit volume than was present in the starting extract. This demonstrates agent concentration on the column under adsorption conditions, followed by a subsequent enrichment of the agent in the eluate. The potency-nitrogen ratios in Table 1 demonstrate the increase in purity of the agent, relative to nitrogen, in the low NaCl eluates. The average was 5.2, with a range from 4.1 to 7.7, or a gain, over the partially purified extract used as starting material, of 310–670%, respectively.

In Fig. 2 it is noted that, in contrast to the regional concentration of the virus in the top of the column, nitrogen unassociated with virus activity is distributed throughout the column and in the filtrate. The agent

TABLE 1

EFFECT OF SALT CONCENTRATION ON QUANTITY OF AGENT AND NITROGEN ELUTED FROM CELITE COLUMNS FOLLOWING DEVELOPMENT

NaCl concentration of eluants		Nitrogen (mg/ml)	Nitrogen (%)	Potency* (%)	Standard error of potency estimate	Potency-nitrogen ratio†	Agent recovered (%)
Molarity	Log molarity						
(Starting extract)		0.0092	100.0	100.0	.....	1.0	100.0
0.01	−2.0	0.0017	18.5	4.0	+ 1.7 − 1.2	0.2	0.8
0.005	−2.3	0.0013	14.1	20.4	+ 7.9 − 5.7	1.5	4.1
0.001	−3.0	0.0017	18.5	92.0	+28.7 −21.9	4.9	18.4
0.0005	−3.3	0.0025	27.2	138.3	+55.5 −39.6	5.0	27.7
0.0001	−4.0	0.0033	35.9	145.7	+56.0 −40.4	4.1	29.1
0.00001	−5.0	0.0024	26.1	198.6	+75.7 −54.8	7.7	39.7
Distilled water		0.0046	50.0	210.4	+82.6 −59.3	4.2	42.1

* Expressed as virus concentration compared with that of the partially purified starting extract. The volume of eluate was 1/5 that of the material originally adsorbed.

† Potency-nitrogen ratio equals per cent potency divided by per cent nitrogen to give an approximate index of purity based on nitrogen.

The difference between 4.1 and unity is highly significant statistically; the difference between 7.7 and 4.1 is not. Statistical counsel was provided by Jerome Cornfield.

[2] The curve in Fig. 1 is the mean of two quantitative experiments. The data of one of these are listed in the table.

particulates associated with chicken tumor I are accordingly segregated from some of the nonvirus nitrogen components of the previously purified extract.

With the growing interest in subcellular particulates—both normal and pathological—the need for techniques which permit the separation of these labile entities becomes more pressing. As partially illustrated above, the method of chromatographic adsorption may be adaptable not only to the separation of pathologic particulates but, perhaps, also to the study of the "normal" submicroscopic particles.

It is to be noted that in the electron microscope studies of the fractions here reported a high concentration of particles was observed in some of the lower segments of the adsorption columns, where no agent activity was present. These were morphologically similar to the particles observed in the top band, where the agent was concentrated.

It is generally recognized that adsorption phenomena (*5*) of some sort influence the passage of viruses through bacterial filters of the Berkefeld type. Since the reported composition of this filter (*10*) is compressed diatomaceous earth, the adsorption curve in Fig. 1 is of interest. The salt concentration in Locke's, Ringer's, Tyrode's, and other isotonic solutions is considerably in excess of the maximum concentration which permits normal passage of the agent through diatomaceous earth. Approximately 99% of the virus from 50 ml of a highly potent extract was removed by passage through 0.5 gm of diatomaceous earth in the column when the salt concentration was −2 log molar, and none the less than 1% would pass into the filtrate at the physiological level of −0.8 log molar. This is in contrast to the relatively free passage at NaCl concentrations of less than −3 log molar (0.001 M). These results enjoin caution in the interpretation of negative filtration results under conditions which prevented the passage of the highly potent agent here studied.

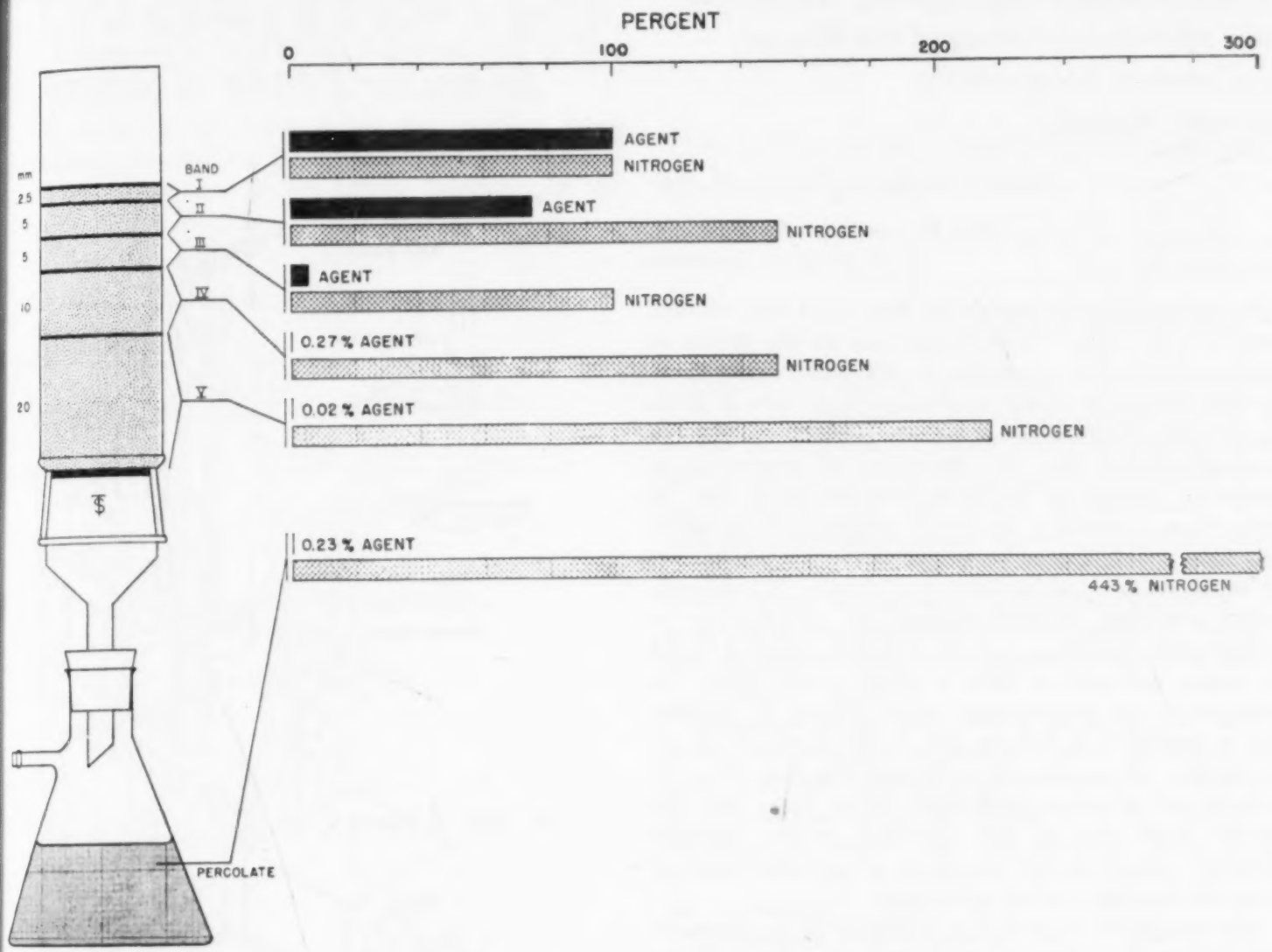


FIG. 2. Segregation of the chicken tumor agent and contaminating nitrogen on silica.

References

1. BEARD, J. W. *J. Immunol.*, 1948, **58**, 49–108.
2. BRYAN, W. RAY. *J. nat. Cancer Inst.*, 1946, **6**, 225–237.
3. BRYAN, W. RAY. *J. nat. Cancer Inst.*, 1946, **6**, 373–377.
4. BRYAN, W. RAY, RILEY, VERNON T., DEIHL, GEORGE D., and VOORHEES, VIRGINIA. *J. nat. Cancer Inst.*, 1947, **7**, 447–453.
5. KRAMER, S. P. *J. inf. Dis.*, 1927, **40**, 343.
6. MARKHAM, R. *Parasitology*, 1944, **35**, 173–177.
7. RILEY, VERNON T., CALNAN, DOROTHY, and BRYAN, W. RAY. *J. nat. Cancer Inst.*, 1946, **7**, 93–98.
8. STRAIN, HAROLD H. *Chromatographic adsorption analysis.* New York: Interscience, 1945.
9. ZECHMEISTER, L., and CHOLNOKY, L. *Principles and practice of chromatography.* New York: John Wiley, 1943.
10. ZINSSER, HANS, and BAYNE-JONES, S. *A textbook of bacteriology.* (7th ed.) New York: Appleton-Century, 1935. P. 1106.

IN THE LABORATORY

An Automatic Proportioning Apparatus for Experimental Study of the Effects of Chemical Solutions on Aquatic Animals[1]

ALBERT COLLIER and SAMMY M. RAY

826 Maison Blanche Building, New Orleans, Louisiana

In carrying out a considerable amount of experimental work in connection with investigations on the effects of industrial pollution on oysters it was found desirable to have an apparatus for the injection of experimental fluids in constant proportions. The requirements of such an apparatus would be: (1) flexibility of proportioning, automatic change of injection with changing flow of water from laboratory sea water supply, and operation over long, uninterrupted periods of time; (2) a minimum of metal surfaces in contact with fluids; (3) dependability and ease of maintenance; (4) adaptability to kymographic recording; and (5) low cost. Also, it would be highly desirable to keep a given oyster under the influence of the experimental fluids as long as possible, with a minimum of fatigue due to the experimental environment. The apparatus to be described here (Fig. 1) fulfilled all of these conditions better than any the authors were able to find described in the scientific literature (*1*) or in the catalogues of manufacturers of commercial proportioning apparatus.

The mechanism in general is a proportioning apparatus activated by the inflow and outflow of water from the sea water supply. This activation occurs by means of a float which operates a ratchet mechanism which in turn lowers a siphon connected to the reservoir containing the experimental fluid. By this arrangement an automatic proportioning is obtained. Each time the float rises and falls a definite amount of experimental substance is delivered from the reservoir, whether or not the float rises and falls fast or slow.

The sequence of events in the operation of the mechanism can be related as follows: The activating float (A) rises with the inflow of water into the metering jar (B). As this happens, the lever (C) lowers and turns the ratchet wheel (D) in a counterclockwise direction. This unwraps the string from the spool (E) and so lowers the block carrying the outlet (F) of the siphon (G) which drains fluid from the reservoir (H). The amount of fluid delivered is dependent entirely on the distance traveled by F on each cycle of the float and the diameter of the reservoir. The distance traveled by F on each cycle can be varied by changes in the diameter of the spool (E) and by the number and size of teeth in the sprocket wheel (D). The drops from F fall into the splashproof con-

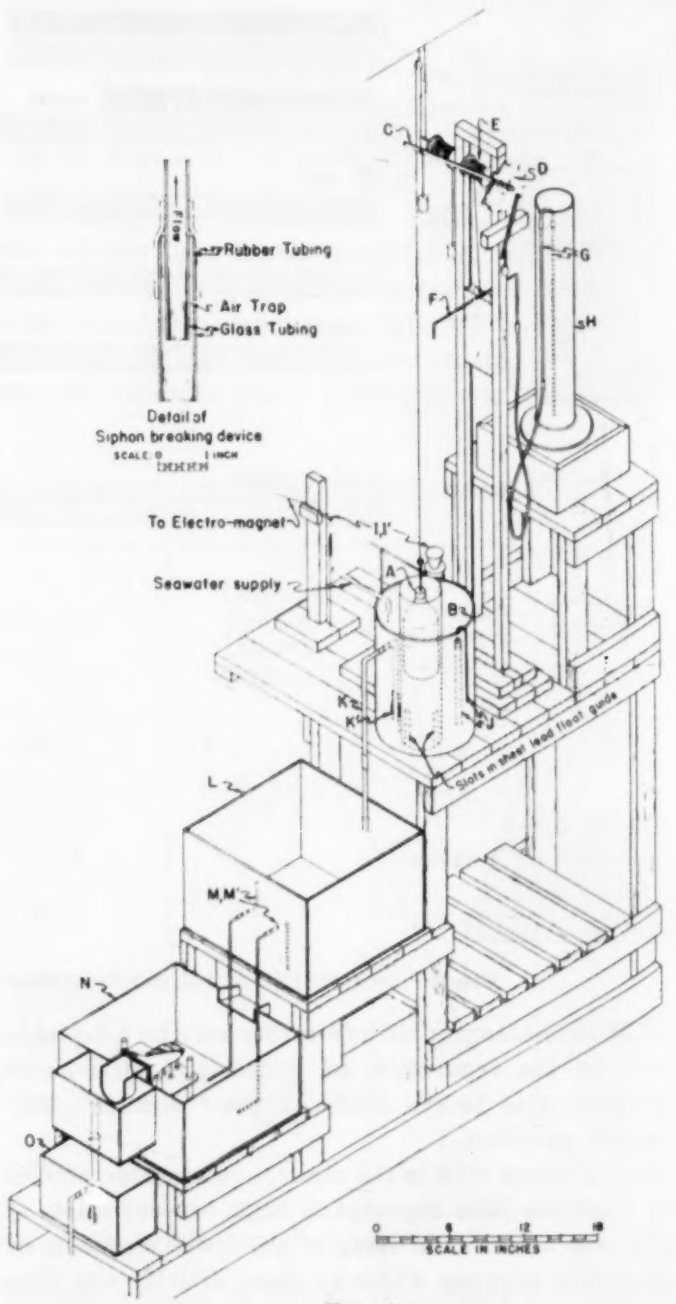


FIG. 1

drop indicator (I, I′) and thence to the metering jar as it fills and where the first mixing occurs. Because of the turbulence within the jar, this mixing is quite thorough. The indicator is wired to an electromagnet which records the inflow of experimental fluid on the kymograph record. The hydrostatic tube (J) is connected to an ordinary recording tambour and transmits the rate of flow of sea water into the metering jar to a recording on the kymograph. Thus, an automatic record is obtained of both the introduction of the experimental fluid and the rate of flow of sea water.

[1] This apparatus was developed by the authors while using space and facilities kindly loaned to them by the U. S. Fish and Wildlife Service at Pensacola, Florida, for the purpose of carrying out independent investigations.

The experimental mixture is in turn delivered from the metering jar to the secondary mixing chamber and accumulator (L) by the automatic siphon (K). K′ is an obvious device at the intake of the siphon to give a clean break of the flow of fluid at the end of a cycle. The principle of this device is gained by the air trap maintained in it as the level of fluid rises.

The accumulator (L) serves two purposes. As already indicated, it gives a secondary mixing and provides a constant flow of water to the experimental animal, thus eliminating the effect of an interrupted flow.

The tubes (M, M′) are siphon and overflow tubes, respectively, to maintain the uninterrupted flow of water from the accumulator to the animal chamber. In this particular case the constant level chamber (N), as developed by Galtsoff (*1*), Nelson, Loosanoff, and others, was used.

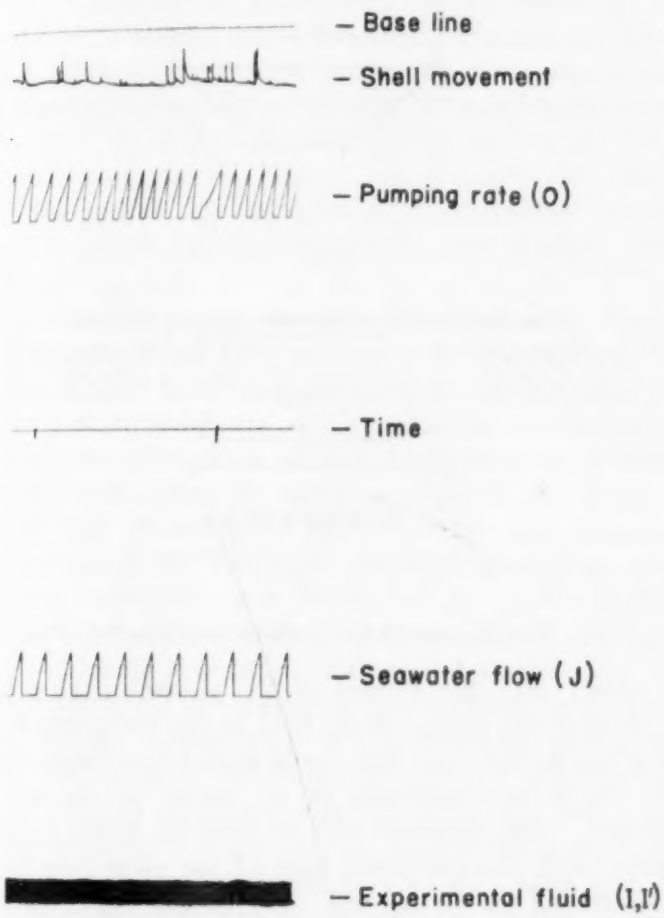


FIG. 2. Sample of record obtained by apparatus described. Letters in parenthesis are reference letters used in text.

In this respect our principal deviation from their developments is the method of measuring the water pumped by the oyster. This, in our case, is simply a receiving chamber (O) provided with an automatic siphon like that described for the metering jar above. The receiving chamber is also equipped with a hydrostatic tube and recording tambour, as above.

The principal criticism of this apparatus would be that the fluids flowing in while the siphons are emptying the respective vessels would not enter into the final aggregates recorded. This, however, is taken care of by calibrations derived from measurements of actual flow from the delivery ends of the siphons while they are in operation. The measuring box for the oyster chamber has the advantage of giving direct information on the minute changes in the pumping behavior of the oyster. This is illustrated in the sample record shown in Fig. 2.

Reference

1. GALTSOFF, PAUL S. Reaction of oysters to chlorination. (Research Rep. 11, U. S. Fish & Wildlife Service, Washington, D. C.)

The Induction of Cytogenetic Variations by Ultrasonic Waves

R. H. WALLACE, R. J. BUSHNELL, and EARL H. NEWCOMER

University of Connecticut, Storrs

Root tips of *Allium* and *Narcissus*, shoot tips of *Helianthus*, and young adults of *Drosophila melanogaster* were treated in an intense ultrasonic field generated by a piezoelectric instrument with an output of approximately 150 watts acoustic (by calorimetric determination) in the zone where the material was exposed. The vibration frequency used was 400,000/sec. Exposures were made in several types of specially constructed chambers. The technic of exposure, although not yet completely standardized, has yielded sufficiently promising results to warrant a preliminary report.

Helianthus plants now growing in the greenhouse after having their apical meristems treated in the seedling stage show definite phenotypic appearances suggestive of genetic changes which are corroborated by cytologic examination of treated root tip material. Some show a hypertrophy and a thickened, rugose condition of the leaves reminiscent of the results of colchicine treatment.

Chromosome examinations of root tip smears and sections show frequent breakage of whole chromosomes and individual chromatids. Late prophase, metaphase, and anaphase chromosomes show an almost complete uncoiling with the chromatids lying parallel, with numerous breaks, attenuations, fusion of parts, and other general evidences of physical disruption. Interphase nuclei often appear as though lysed and are sometimes extended the length of the cell in a spiral form. The nuclear membrane of such deformed nuclei in some cells is destroyed; in others it appears to be intact. In some cells the interphase nuclei, nucleoli, and the cytoplasm were completely segmented into two to four integral parts. Spindle figures of dividing nuclei in affected areas seem to be totally destroyed.

Despite the observed general disruption of the cell system, recovery as measured by resumption of growth seems to be general in all but those tissues which showed general collapse by the longer exposures. In collapsed tissues, no evidences of discrete or dispersed nuclei could be found by staining.

Young adult flies, etherized just prior to treatment, show effects ranging from none through phenocopy in-

duction, mutations of both lethal and visible types, sterility, and death, depending upon the time and technics of exposure. More tests were made with the CLB method, whereby an analysis was made of effects on the X chromosome in the sperm of the treated males. The effects observed in this test include lethal mutations, visible mutations affecting the wings, and inversions, as determined by cross-over tests. The frequent finding of unilateral wing mutations in the F_2's suggest that most CLB or other tests should be carried through the F_3 generation. Treated females carrying recessive genes show increased rates of primary nondisjunction of the sex chromosomes.

More detailed accounts of these investigations will be published elsewhere at a later time. The authors are indebted to S. I. Ward, president of the Crystal Research Laboratories of Hartford, Connecticut, for the loan of the ultrasonic equipment used in this research.

A Rapid Method of Single Cell Isolation

RICHARD D. NORTHCRAFT

Department of Botany, Rutgers University

During the course of an investigation on *Chlamydomonas* it became necessary to isolate particular zygotes. A simple, accurate method was developed, based on variations of the principles used by Edgerton (*2*), La Rue (*3*), and Dickinson (*1*). The present method requires the construction of two special instruments, a marking device and a supporting slide.

One part of the marking device was made from a sheet of Lucite 1.5 mm thick. A circular disc (E) was cut and ground to a diameter equal to the width of the flat lens surface of the Abbé condenser on a compound microscope. A small hole about 0.5 mm in diameter was then drilled in the exact center of the disc. The other part of the marking device consisted of a small-bore glass tube (D), the diameter of which was somewhat less than the width of the visual field of the compound microscope. Pyrex glass tubing with an outside diameter of 5.0 mm was drawn out to 0.5 mm diameter over a Bunsen burner and fractured so that a sharp, clean, 90° angle was obtained. The tip was then sharpened by rotating the fractured end of the glass tube between a carborundum stone and forefinger until a good cutting angle was obtained. After fracturing the glass tubing about 3.0 mm from the sharpened tip, the newly fractured end was glued into the hole, in the center of the Lucite disc (Fig. 1). The assembled piece was mounted on the lens of the Abbé condenser and the upthrust cutting edge centered in the visual field of the microscope. A drop of glycerin on the surface of the lens acted to stabilize the instrument and clarify the optical system. Ultraviolet light was used to sterilize the sharpened tip before it was used.

The supporting part of the apparatus (B) consisted of a piece of Lucite cut to the same dimensions as a standard glass microscope slide. From the center a 15.0-mm-square segment was removed.

A piece of sterile 4.0% agar (C) about 10.0 mm square and 0.5 mm thick is placed in the center of a cover slip 22.0 × 40.0 mm (A). The cells to be isolated are gently streaked with an inoculation needle onto the surface of the agar square. The cover slip with the inoculated agar square is inverted and centered in the window of the Lucite slide, a drop of glycerin on each end of the cover slip serving to anchor it to the slide. The whole mount is then placed on the stage of the microscope and the cells observed *through the agar* with the low-power objective (about 100 ×). Each cell may be studied under high power for further determination of its suitability for isolation. When a desirable cell is located, the condenser

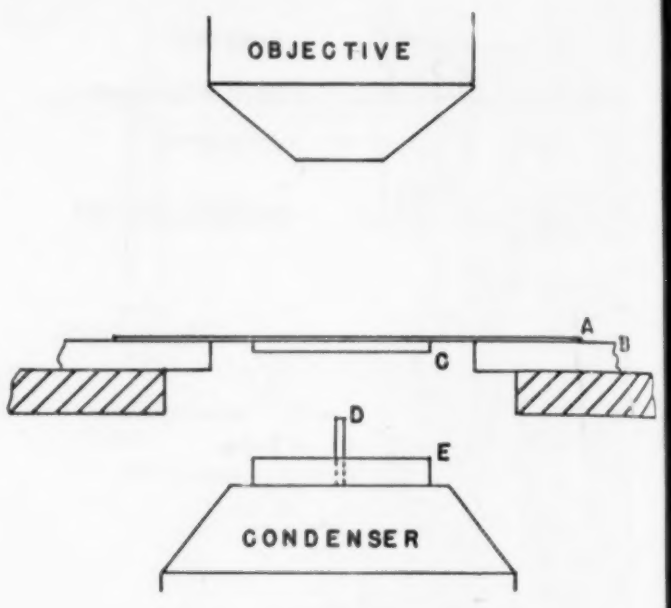


FIG. 1. Assembled isolation apparatus.

is raised until the shadow of the ascending glass tube appears in the center of the field of the low-power objective, the Lucite slide then being moved horizontally until the cell is approximately in the center of the circular shadow. The condenser with its marking device is slowly raised until the sharpened edge of the glass tube cuts a ring around the desired cell. The cutting edge is worked upward until it rests against the cover slip so that the agar plug and its cell are thus completely severed from the surrounding agar. The process of "ringing" cells may be repeated several times on the same piece of agar.

After the cells are marked, the cover slip with the agar square is placed, agar side up, on the stage of a binocular dissecting microscope, and the agar plug, together with the accompanying cell, is removed with a platinum-iridium microscalpel and placed on a suitable culture medium.

The method described is effective in the isolation of very small cells (about 2.0 μ). By this procedure 30 or more single cell isolations may be made in 1 hr. Also a particular cell may be studied in detail at a magnification up to 800 × prior to isolation. The apparatus is made from materials available in any biology laboratory.

References

1. DICKINSON, S. *Phytopathology*, 1933, **23**, 357.
2. EDGERTON, C. W. *Phytopathology*, 1914, **4**, 115.
3. LA RUE, C. D. *Bot. Gaz.*, 1920, **70**, 319.

Book Reviews

Surface chemistry for industrial research. J. J. Bikerman. New York: Academic Press, 1948. Pp. ix + 464. (Illustrated.) $8.00.

The writing of this book was an ambitious undertaking in which the author sought to show the applications of the fundamental theories pertaining to surfaces, to natural phenomena, and to industrial processes. The scope of the work is nearly as broad as that covered in Volumes I, III, IV, and VI of Alexander's *Colloid chemistry*.

The book is divided into 6 chapters. The chapter headings, number of pages, and number of references in the extensive bibliographies at the end of each chapter, are listed here in that order: "Liquid-Gas," 114, 297; "Liquid-Liquid," 39, 122; "Solid-Gas," 76, 193; "Solid-Liquid," 72, 187; "Solid-Liquid-Gas. Solid-Liquid-Liquid," 47, 134; and "Electric Surface Phenomena," 54, 111.

Fundamental theory for the liquid-gas and liquid-liquid interfaces and brief reviews of 12 or more methods of experimental study and measurement are given in 22 pages, most of which are at the beginning of Chapter I. Although the treatments are not as rigorous or as thorough as those given in such books as N. K. Adam's *Physics and chemistry of surfaces*, they will probably be satisfactory for the great majority of readers, and the many references make it easy for any reader to find more detailed and comprehensive treatments of any subject in which he may be particularly interested.

In pointing out the industrial applications, little or no space is used in explaining or describing the industrial procedures as such. The applications will therefore be best understood and appreciated by those who either are already familiar with the various steps in the procedures in which they are interested or who will make use of some other work to obtain the required details of procedure. This, of course, makes possible the covering of a wide range of subjects on relatively few pages, but it also means that a person interested in one particular industry will find relatively few pages concerned with his particular field. It does not follow, however, that the value which such a reader will receive is small because the number of pages is small. There is a decided advantage in having the application discussed clearly and briefly instead of being scattered through many pages of descriptive material.

One of the most valuable features of the book is the very extensive bibliography to which numerous references are made throughout the text. The treatment of the characteristics of solid surfaces, especially in regard to their smoothness and other factors which determine the contact angles which liquids make with the solids, is unusually thorough.

The work, in common with most works, has some faults. Most of these are the result of too great a condensation of material in the development of equations and concepts. Early in the book (pp. 3–4), in presenting an aid for remembering the fundamental equation which relates the pressure inside of a bubble to the radius of the bubble, the author twice uses the statement, "The more crowded the radii the higher the pressure." To show this, he draws portions of two circles of slightly different diameters; one is concave downward and contains three radii 60° apart; the other is concave upward and contains four radii 60° apart. It would seem that he should explain that by "crowded" he means that the chord, or its subtended arc, formed by the radii intersecting the circle is less when the radii are shorter. However, there would be little need for this memory aid if a more complete explanation of why there is a pressure difference had been given.

In the index the subject "Gibbs Adsorption Theorem" is followed by references to pages 64 and 150. On each of these pages brief references are made to applications of the theorem. One of these pages contains a reference to paragraph 50 on pages 82–83, where a fairly complete discussion of the theorem is given. It is obviously an oversight that this longer treatment was not listed in the index.

Generally, however, the reviewer feels that the terseness, clarity of expression, and brief, pointed descriptions of applications of fundamental theory constitute the strongest and most characteristic features of the book. It is a valuable addition to our list of books dealing with colloid chemistry and deserves a place in every reference library concerned with that subject.

E. ROGER WASHBURN

University of Nebraska

Microwave mixers. Robert V. Pound (with a chapter by Eric Durand). (Ed. by C. G. and D. D. Montgomery.) (Massachusetts Institute of Technology Radiation Laboratory Series.) New York-London: McGraw-Hill, 1948. Pp. xii + 381. (Illustrated.) $5.50.

This book presents the first collected data of a new art—that of the conversion frequency problem for microwave frequencies. This is a subject that was newborn out of the recent war. Whereas some of the previous volumes of this series tend to present the broad phases of microwave systems in semitechnical form, this volume treats a specialized portion of the microwave picture and subjects it to microscopic scrutiny. The purpose of such a thorough analysis is to yield data on microwave mixers sufficiently complete for design purposes.

The book is profusely illustrated with many perspective views and cross-sectional drawings of representative mixer assemblies. Dimensioning of the sectional drawings emphasizes very graphically the physical size and appearance of the "plumbing." The particular assem-

blies described were restricted to some of the designs evolved at the Radiation Laboratory and cannot, therefore, be considered to be the only practical ones. However, the examples cited are sufficiently varied to fire the imagination of the designer and give him a starting point.

The chapter on "Crystal Rectifier Units" does not cover crystal rectifiers in great detail. However, a sufficiently complete discussion is presented to lay the groundwork for a better understanding of the remainder of the book. A linear-network analysis of crystal frequency conversion, a description of noise-temperature measurements, and a table of commercial crystal types are included in this chapter.

The origin of superheterodyne receiver noise arising in the local oscillator is examined, and means for minimizing its effects by proper mixer design are treated. The design of balanced mixers is developed in detail.

A lengthy chapter, authored by Eric Durand, on "Local Oscillator Frequency Control" covers A.F.C. principles, suitable discriminator types, various hunting systems, and oscillator control circuits. Since it may be easily overlooked in this volume, it appears that this subject would be more in place in the volumes of this series devoted to receiver and oscillator design.

Descriptions of measurement techniques peculiar to microwave converters conclude the volume.

The book as a whole is well written and concise. Because of the limited subject and the very specialized subject matter, it may be considered a valuable reference source rather than a text.

GUSTAVE SHAPIRO

National Bureau of Standards

Scientific Book Register

ASTALDI, G., and BALDINI, M. *Il principio antianemico-pernicioso: natura, meccanismo d'azione, dosaggio.* Pavia, Italy: Il Farmaco Scienza e Tecnica, 1948. Pp. 234.

BAILEY, ALTON E. (Ed.) *Cottonseed and cottonseed products: their chemistry and chemical technology.* New York-London: Interscience, 1948. Pp. xxiii + 936. (Illustrated.) $17.50.

BEQUAERT, JOSEPH C. *Monograph of the Strophocheilidae, a neotropical family of terrestrial mollusks.* (Vol. 100, No. 1.) Cambridge, Mass.: Museum of Comparative Zoölogy, 1948. Pp. 210. (Illustrated.)

BUZZATI-TRAVERSO, ADRIANO, and CAVALLI, LUIGI L. *Teoria dell'urto ed unita biologiche elementari.* Milan, Italy: Longanesi, 1948. Pp. 254. (Illustrated.) 600 lire.

FROCHT, MAX MARK. *Photoelasticity.* (Vol. II.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. xvii + 505. (Illustrated.) $10.00.

GOLDSMITH, ALFRED N., *et al.* (Eds.) *Frequency modulation.* (Vol. 1.) Princeton, N. J.: RCA Review, 1948. Pp. x + 515. (Illustrated.) $2.50.

HARRISON, BRUCE M. *The dissection of the cat (Felis domestica): a laboratory manual.* St. Louis, Mo.: C. V. Mosby, 1948. Pp. 109. (Illustrated.) $3.50.

KELLY, EMERSON CROSBY. *Encyclopedia of medical sources.* Baltimore: Williams & Wilkins, 1948. Pp. v + 476. $7.50.

KING, HORACE W., WISLER, CHESTER O., and WOODBURN, JAMES G. *Hydraulics.* (5th ed.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. xii + 351. (Illustrated.) $4.00.

MOREHOUSE, LAURENCE E., and MILLER, AUGUSTUS T. *Physiology of exercise.* St. Louis, Mo.: C. V. Mosby, 1948. Pp. 353. (Illustrated.) $4.75.

RIDER, JOHN F., and USLAN, SEYMOUR D. *FM transmission and reception.* New York: John F. Rider, 1948. Pp. vi + 409. (Illustrated.) $1.80, paper; $2.70, cloth.

RUNES, DAGOBERT D. (Ed.) *The diary and sundry observations of Thomas Alva Edison.* New York: Philosophical Library, 1948. Pp. xii + 247. (Illustrated.) $4.75.

SEWELL, R. B. SEYMOUR. *The free-swimming planktonic Copepoda: systematic account.* (The John Murray Expedition, 1933–34, Sci. Reps., Vol. VIII, No. 1.) London: British Museum (Natural History), 1947. Pp. 303. (Illustrated.) 1£ 10/.

SMITH, SYLVANUS J. *Introductory chemical calculations.* New York: Macmillan, 1947. Pp. vii + 144. $1.00.

TANNER, FRED WILBUR, and TANNER, FRED WILBUR, Jr. *Bacteriology: a textbook of microorganisms.* (4th ed.) New York: John Wiley; London: Chapman & Hall, 1948. Pp. x + 625. (Illustrated.) $4.50.

TOKSVIG, SIGNE. *Emanuel Swedenborg, scientist and mystic.* New Haven: Yale Univ. Press, 1948. Pp. 380. (Illustrated.) $5.00.

VAN VOORHIS, S. N. (Ed.) *Microwave receivers.* (MIT Radiation Laboratory Series.) New York-Toronto-London: McGraw-Hill, 1948. Pp. xviii + 618. (Illustrated.) $8.00.

VESTINE, E. H., *et al.* *The geomagnetic field, its description and analysis.* (Publ. 580.) Washington, D. C.: Carnegie Institution of Washington, 1947. Pp. vi + 390. (Illustrated.) $1.85, paper; $2.40, cloth.

VOGEL, ARTHUR I. *A text-book of practical organic chemistry including qualitative organic analysis.* London-New York-Toronto: Longmans, Green, 1948. Pp. xxiii + 1012. (Illustrated.) $10.00.

WILLIAMS, R. TECWYN. *Detoxication mechanisms: the metabolism of drugs and allied organic compounds.* New York: John Wiley, 1947. Pp. viii + 288. $5.50.

WILLIS, R. A. *Pathology of tumours.* London, Engl.: Butterworth; St. Louis, Mo.: C. V. Mosby, 1948. Pp. xxiii + 1044. (Illustrated.) $20.00.

WREDDEN, J. H. *The microscope, its theory and applications.* New York: Grune & Stratton, 1948. Pp. xxiv + 296. (Illustrated.) $5.50.

ZELIFF, C. COURSON. *Laboratory manual for introductory zoology.* (Rev. ed.) State College, Pa.: W. B. Keeler College Book Stores, 1948. Pp. 154. (Illustrated.) $2.75.